ACTA RADIOLOGICA
EDITA PER SOCIETATES RADIOLOGICAS DANIÆ, FENNIÆ, HELVETIÆ, HOLLANDIÆ, NORVEGIÆ ET SUECIÆ

VOL. XXXII FASC. 5—6 31 : XII 1949 N:o 189—190

SUBCLAVIAN ANGIOGRAPHY BY ARTERIAL CATHETERIZATION[1]

Visualization of Metastatic Tumor in the Upper Thoracic Aperture

by

Stig Radner

Since the introduction of the roentgenographic visualization of the arteries of the extremities by BERBERICH & HIRSCH in 1923 the same principle of examination has been applied by a large number of investigators to most parts of the cardiovascular system. The technique of injection of the radiopaque material is determined by the structures to be visualized. As a principle the direct injection of this material into the cardiovascular section concerned may be considered the method of choice. In case of deep-seated cardiovascular structures, however, the direct technique of injection may be met with difficulties.

Previous Experiences on Visualization by Catheterization

Visualization by Venous Catheterization. In 1931 FORSSMANN reported the results of the injection of radiopaque material into the right side of the heart after catheterization. The catheter was inserted into a cubital vein and passed via the veins of the upper extremity and the superior vena cava into the right auricle. The purpose of this procedure was to visualize the right side of the heart and the pulmonary circulation, but no distinct visualization was obtained. — In 1932 de CARVALHO, MONIZ & SALDANHA described the same technique of injection for the investigation of the pulmonary vasculature. They succeeded in visualizing the pulmonary arterial system, but the results achieved by these and other authors, using a similar technique, *e. g.* AMEUILLE, RONNEAUX, HINAULT and DESGREZ in 1938, apparently were of limited

[1] Submitted for publication, Aug. 24, 1949.

From the Roentgen-Diagnostic Department (Tempor. Head: OLLE OLSSON, M. D.), and the Medical Clinic (Tempor. Head: KNUT LIEDHOLM, M. D.), University Hospital of Lund, Sweden.

diagnostic significance. The lastmentioned authors in some cases also visualized the right cavities of the heart.

A modification of the catheterization technique of FORSSMANN was described by ARA in 1931. The catheter was inserted into the internal jugular vein and passed through the superior vena cava into the right side of the heart. After the injection of contrast material through the catheter he obtained »very clear visualization of the lung vessels». In 1947 CHÁVEZ, DORBECKER and CELIS reported their results with the technique of ARA, modified only by entering the external instead of the internal jugular vein. Good visualization of the right and left cavities of the heart, the pulmonary vessels and the thoracic aorta was obtained.

Visualization by Arterial Catheterization. In 1941 FARIÑAS described his method for abdominal aortography by catheterization. The femoral artery was exposed and punctured with a trocar through which a catheter was passed and introduced to the desired level in the abdominal aorta. Contrast material then was injected through the catheter. Good aortograms were achieved. The method of FARIÑAS apparently has not been used by other investigators.

A method for vertebral angiography by catheterization was described by RADNER in 1947. After exposure of the radial artery a catheter was introduced in retrograde direction via the brachial, axillary and subclavian arteries into the vertebral artery whereupon contrast material was injected through the catheter. This method now has been applied by us in 142 instances without untoward effects so far due to the catheterization. The insertion of the catheter into the vertebral artery, using this technique, is practicable in more than 95 per cent of all cases in the ages of one and a half to seventy-six years.

Thoracal aortography by catheterization from the radial artery was introduced by RADNER in 1948. The method was used by BRODÉN, HANSSON and KARNELL (1948) to the diagnosis of aortic malformations and by JÖNSSON (1948) for the visualization of the coronary arteries.

Subclavian Angiography by Arterial Catheterization

From the deeply placed medial portion of the subclavian artery branches arise which supply important structures. The parathyroid glands, the posterior and lower part of the thyroid gland, and the thymus gland are supplied from this section of the artery. Angiography by the injection of contrast material into the subclavian artery is proposed to the visualization of lesions, principally tumors, of the structures mentioned above. As the injection is not made directly into the supplying branches a high concentration of the radiopaque substance in the main

trunk is necessary. In my opinion this is best achieved by the injection through a catheter which is placed in the main trunk. The direct puncture and injection into the subclavian artery postulates a relatively coarse needle to get adequate filling, and untoward effects may occur in the use of such a procedure. The catheterization is painless and without danger, and it ensures a complete filling.

Technique. In order to prevent arterial spasm 8—10 cc. of a 2.5 per cent solution of papaverin hydrochloride are injected intramuscularly in adult subjects one hour before the catheterization. The dose should be duly reduced in lower ages. Morphium or a similar preparation should also be given prophylactically for the transient pains following the injection of the contrast substance. Under strict aseptic precautions and using local anesthesia, the radial artery is exposed and ligatured in the proximal part of the forearm. A second ligature is placed loosely proximally to the first ligature. A small incision is made in the artery between the ligatures, the proximal being drawn to strangulate the artery temporarily. A ureteral catheter is inserted through the incision and guided under fluoroscopic control into the subclavian artery. The catheter unit described by RADNER in this journal in 1949 may be used. The catheter should be as coarse as is conveniently permitted by the size of the radial artery, usually French 6—9 in adult subjects.

When the catheter is introduced into the subclavian artery a sphygmomanometer cuff is placed on the brachium and insufflated to a pressure somewhat exceeding the systolic blood pressure. Fifteen cc. of 35 per cent solution of Umbradil (Astra) then are injected as rapid as possible, and two pictures are taken: one at the completion of the injection and one 3—4 seconds later.

After the withdrawal of the catheter also the proximal ligature is drawn. — No vascular disturbances have been encountered following the ligature of the radial artery.

Illustrative Case. Woman, aged 56. In 1936 a hypernephroma of the left kidney was diagnosed and nephrectomy was carried out. — In 1948 roentgen examination showed a destructive lesion in the lumbar vertebral column, suggestive of a metastatic involvement or, alternatively, osteitis fibrosa. As there was also a very high calcium level in the blood, sometimes 17 milligrams per cent, and as so long time had elapsed since the nephrectomy, the presence of a parathyroid adenoma had to be excluded. In August 1948 a surgical exploration of the parathyroid glands was performed, but no adenoma was found. — The general condition of the patient gradually was impaired and destructive lesions, similar to those in the lumbar region, appeared in the thoracic vertebral column.

In May 1949 subclavian angiography by arterial catheterization was carried out on both sides in order to visualize the circulation of the parathyroid glands. On the right side a walnut-sized system of pathological vessels was recognized (Fig. 1). On the left side an essentially normal picture was obtained (Fig. 2).

Fig. 1 a. Catheter introduced into the right subclavian artery and diodrast injected through the catheter. Picture taken at the completion of the injection. Visualization of the subclavian circulation and of a walnut-sized system of pathological vessels.

Fig. 1 b. Picture taken four seconds after 1 a. Contrast material in scattered areas of pooling, corresponding to the pathological vascular system of 1 a.

Exploration of the right supraclavicular fossa was performed (Prof. J. P. STRÖMBECK) and a tumor was found, corresponding as to its size and location exactly to the pathological vasculature on the roentgen picture. The tumor was deeply situated, lying posteriorly

Fig. 2. Essentially normal subclavian angiographic anatomy on the left side.

to the vertebral artery. This artery had to be ligatured and divided for the approach to the tumor. The tumor then was easily extirpated.

The tumor was soft and it had a thin capsule. The cut surface had a granulated appearance and the color was yellowish brown.

Following the operation the patient developed signs of intracranial complication. A positive Babinski's reflex, facial weakness and a Horner's syndrome were encountered on the right side. She was very drowsy and gradually she lost consciousness and died, on the second day after the operation.

Autopsy (Prof. C. G. AHLSTRÖM) revealed general hypernephroma metastases in the vertebral column, in the pituitary gland, etc. The microscopic examination of the tumor extirpated from the right supraclavicular fossa showed the same pathological picture as in the metastases, the tumor also being a metastasis from the hypernephroma.

This method of visualization has been so far applied in one case only, but its further use is intended.

SUMMARY

Previous experiences on the catheterization technique for radiographic visualization are reviewed.

A method is proposed to the angiographic investigation of the structures supplied from the medial portion of the subclavian artery, *e. g.* the parathyroid glands, parts of the thyroid gland and the thymus gland. The subclavian artery is catheterized and contrast material injected through the catheter.

An illustrative case is described in which a metastatic tumor in the upper thoracic aperture was visualized by this method.

ZUSAMMENFASSUNG

Frühere Erfahrungen inbezug auf die Technik der Katheterisierung zwecks röntgenologischer Darstellung werden durchgenommen.

Es wird eine Methode vorgeschlagen zur angiographischen Untersuchung derjenigen Strukturen, die von der mittleren Partie der Art. subclavia aus versorgt werden, so z. B. der Nebenschilddrüsen, Teilen der Schilddrüse und des Thymus. Die Art. subclavia wird katheterisiert und durch den Katheter Kontrastmittel eingespritzt.

Ein anschaulicher Fall wird beschrieben, bei dem ein metastatischer Tumor der oberen Brustapertur mit dieser Methode sichtbar gemacht wurde.

RÉSUMÉ

Revue des expériences antérieures faites avec la technique destinée à obtenir des images radiographiques par cathétérisme.

L'auteur propose une méthode d'examen angiographique des organes irrigués par la partie interne de l'artère sous-clavière, par ex. les glandes parathyroïdes, des portions de la thyroïde, ainsi que le thymus. On cathétérise la sous-clavière et l'on injecte la substance de contraste à travers la sonde.

Description d'un cas où une tumeur métastatique au niveau de l'entrée supérieure du thorax fut rendue visible par ce procédé.

REFERENCES

AMEUILLE, RONNEAUX, HINAULT and DESGREZ: Journ. de Radiol. 1938, 22, p. 97.
ARA, P.: Cit. after CHÁVEZ, DORBECKER and CELIS.
BERBERICH and HIRSCH: Klin. Wchnschr. 1923, p. 2226.
BRODÉN, HANSSON and KARNELL: Acta radiol. 1948, 29, p. 181.
DE CARVALHO, MONIZ and SALDANHA: Journ. de Radiol. 1932, 16, p. 469.
CHÁVEZ, DORBECKER and CELIS: Amer. Heart Journ. 1947, 33, p. 560.
FARIÑAS, P. L.: Amer. Journ. Roentgenol. 1941, 46, p. 641.
— Amer. Journ. Roentgenol. 1946, 55, p. 448.
FORSSMANN, W.: Klin. Wchnschr. 1929, p. 2085.
— München. med. Wchnschr. 1931, p. 489.
JÖNSSON, G.: Acta radiol. 1948, 29, p. 536.
RADNER, S.: Acta radiol. 1947, 28, p. 838.
— Acta radiol. 1948, 29, p. 178.
— Acta radiol. 1949, 31, p. 152.

FROM THE RADIUM CENTRE, AARHUS, DENMARK (CHIEF: PROF., DR. MED. CARL KREBS)

EXTRAMEDULLARY PLASMOCYTOMAS[1]

by

Poul E. Andersen

Under the term »plasmocytomas» or »plasmomas» several pathologic conditions have been collected which are all characterized by a plasma cell proliferation of more or less neoplastic nature.

Well-known are 1) the myelomatosis (multiple myeloma) which is one of the most frequently occurring tumours of bone, 2) the solitary myeloma which is a very rare bone tumour (cf. BICHEL and KIRKETERP), and 3) the plasma cell leukemias which are also very rare (PATEK and CASTLE, REITER and FREEMAN). But besides these diseases which essentially are characterized by their localization to bones and bone marrow, there is one group more: the extramedullary plasma cell tumours. These tumours occur so seldom that no clinic has been able to collect more than a few cases. Therefore most literature on these diseases consists of reports of single cases and most textbooks on pathologic anatomy have only a few remarks on these tumours (10, 15, 28, 50, 62). On the basis of 8 cases treated during the last 6 years at the Radium Centre, Aarhus, a short review of the extramedullary plasma cell tumours will be given followed by short case reports of this material which is one of the largest collections of cases since the first case reported by SCHRIDDE 1905.

Extramedullary plasmocytomas are tumours most frequently met with in men in the decades between 40 and 70 years (GORMSEN: 82 %). 1943 HELLWIG, who also found a great majority of male patients, collected and analysed 127 cases reported in literature and added one case of his own. From that time further c. 50 cases have been reported in the literature accessible to the author and so the total of cases reported together with the author's 8 cases is now approaching 200. The largest collection of cases is from the Mayo clinic and comprises 11 cases (15).

By far the majority of cases (STOUT and KENNEY 1949: 104 cases) has been situated in the upper air passages or the oral cavity which together with the conjunctiva are the sites of predilection for these

[1] Submitted for publication, Aug. 10, 1949.

tumours. 15 cases have originated from the tonsils or lymph nodes while 21 cases have been situated in other organs (stomach, intestines — as a rule ileum —, ovary, thyroid gland, breast, pleura and mediastinum, kidney and skin). Outstanding publications on these tumours have been made by the following authors: FIGI, BRODERS and HAVENS, GORMSEN, HELLWIG, JAEGER, STOUT and KENNEY.

As the above figures show, plasmocytomas are rare tumours and especially when located outside the upper air passages and the conjunctiva exceedingly rare. Among the author's cases is one case situated in the submaxillary region, probably in a lymph node, one case originating from the testis and one case localized to the cervix uteri, a localization which has never before been reported in the literature.

BOIT 1907 appears to be the first author using the term »plasmocytoma» in reporting a case involving the larynx, while the term »plasmoma» was used as early as 1891 by UNNA when discussing the massive plasma cell infiltration seen in lupus vulgaris.

Histology. The joint histologic characteristic of these rare and peculiar tumours is, as seen from their name, plasma cells of typical or more or less atypical appearance, sometimes approaching the appearance of lymphocytes and lymphoblasts, lying in a generally very delicate, sometimes however somewhat granulomatous stroma. Based upon the histologic appearance, especially that of the stroma, the extramedullary plasma cell tumours have been divided into 3 different groups, 1) a group of granulomatous tumours or chronic inflammatory conditions, 2) a group of plasmocytomas — the rarest ones — which as well histologically as clinically very closely resembles Hodgkin's disease and probably is to be interpreted as an atypical plasma-cellular variety of Hodgkin's disease, and finally 3) the true extramedullary plasmocytomas, comprising as well benign — as a rule appearing as mucosal polyps — as more or less malignant, solitary or multiple tumours, polyps or infiltrations, which sometimes involve the regional lymph nodes and perhaps even the bone system in the final stages. The bone metastases resemble very strikingly those seen in multiple myeloma. A few authors will not have observed (f. e. 17) that any of these tumours may be benign granulomatous or inflammatory, but are of the opinion that they must always be regarded as definitely malignant.

The histologic appearance of the 3 groups shall be reviewed shortly. The first mentioned group, granuloma plasmacellulare (KUSUNOKI and FRANK) or inflammatory plasmocytoma, comprises cases, the stroma of which is a granulation tissue entirely dominated by plasma cells. Especially in the centre these tumours or granulomas often consist almost exclusively of typical plasma cells in a very delicate stroma of capillaries

and a little connective tissue while the periphery has a more granulomatous character with numerous capillaries, plasma cells, lymphocytes and leucocytes as seen in chronic and subchronic inflammations. It is well-known that the conjunctiva and the mucosa of the upper air passages in chronic inflammation react with an exceedingly heavy plasma cell infiltration (f. e. in allergic conditions, plasma-cell conjunctivitis, trachoma etc.) and the inflammatory processes are often rather proliferative. A great proportion of the reported cases localized in the conjunctiva and the upper air passages undoubtedly is to be classed in this group as far as can be seen from the reports.

Plasmocytomas of the conjunctiva are found in young persons and often in women. So HELLWIG finds an average age of c. 37 years among 29 cases and a male/female ratio of c. 1. The most frequent localization is the superior palpebra, but all localizations in the conjunctiva have been reported, as well as both palpebrae, both eyes etc. (20, 23, 28, 30, 41, 48). In a very great proportion of the cases the plasmocytomas have been preceded by trachoma (JAMES: 50 %), and KREIBIG has only in 4 out of 46 cases of conjunctival plasmocytoma been able to exclude trachoma. In the same direction points the fact that by far the majority of the cases is reported from countries in which trachoma is a very common disease of the eyes. Clinically the tumours appear as diffuse swellings, more cylindric masses or elevated, sometimes pedunculated smooth, seldom papillary or lobulated, firm tumours. In the histologic specimen is seen a diffuse poorly circumscribed plasma cell infiltration sometimes with large plasma cells with multiple nuclei. As a rule mitotic figures are only few or completely absent. In some cases Russell bodies have been described as well as amyloid changes and hyaline degeneration. Secondary deposits have only been reported in one case (MONTPELIER, CHOUSSAT and SEURAT, cited from GORMSEN), which seems to prove that these tumours are benign granulomas or chronic inflammations.

Besides the localization in conjunctiva and upper air passages granuloma plasmacellulare has been seen in most other regions and organs, most frequently the lips, gingiva, genitals and breasts in which they have a close resemblance to carcinoma, often involving the regional lymph nodes too (1, 14, 21, 37, 47).

The above group 2, plasmocytomas resembling Hodgkin's disease, comprises only a few cases (24, 32, 38, 58, 59) which seem to be partly cases that really are to be interpreted as evident malignant lymphogranulomatosis Hodgkin-Sternberg, only with a very heavy infiltration of plasma cells (as reported f. e. by 12, 27, 18, 40), and partly cases that are true extramedullary plasmocytomas with generalization within the lymphatic system (58) and consequently are to be included in the following group.

Group 3, the proper extramedullary plasmocytomas, is as a rule situated in the upper air passages, the oral cavity, the cervical lymph nodes and the intestines (about 85 % of all the cases; reviews: 20, 23, 55). Macroscopically they are often polypoid or pedunculated when relatively benign, but more infiltrating, invading and ulcerating when malignant. Histologically the outstanding feature is a delicate stroma of capillaries and a fine fibrillar connective tissue in which lie an abundance of plasma cells in massive clusters or sheets and a total lack of inflammatory reaction. Polymorphonuclear leukocytes, histiocytes and lymphocytes, if present at all, never form an essential part of the tumour structure. The round, oval or polygonal tumour cells are characterized by a large amount of basophilic cytoplasm and a usually eccentrically situated large nucleus with the chromatin arranged in cartwheel fashion and a paranuclear unstained area. When clinically malignant more atypical cell structures, a greater variation in size and form of the cells and nuclei, and more mitotic figures are usually seen, but these histologic criteria are not always pronounced. Some cases present clinical evidence of high grade malignant cancer, although the biopsy specimen shows a quite uniform cell structure (50).

Macroscopically, the tumours may be solitary, multiple or generalized, then usually first involving the regional lymph nodes and later on especially the bones. Further they are characterized by frequently occurring in those places in which abundant lymphatic tissue is found, and their involvement of lymph nodes is relatively frequent (17, 20, 53), especially when originating in the tonsils, the base of the tongue and the nasopharynx. It may be noted that in multiple myeloma lymph node metastases are exceedingly rare. On the other hand metastases to liver, lung, kidney etc. are rare findings in as well cases of multiple myeloma as extramedullary plasmocytomas. CUTLER has reported a case with metastases to the breast, RINGERTZ to the skin, MILIAN to the kidney, PINEY and RIACH to pancreas, suprarenal gland, lung and uterus.

Almost 45 % of the proper plasmocytomas have proved to be benign, and about 15 % have been multiple (8, 22, 30, 60). Their site of predilection is the upper air passages, and they are most common in men 55—60 years old (23). The tumours are firm, yellowish gray or — more rarely — bluish red, polypoid or lobulated, pedunculated and often rather large, sometimes the size of an egg (3, 17, 31) and f. e. filling the whole nasopharynx; more infrequently they have been diffuse infiltrates in the mucosa. The multiple benign plasmocytomas are rather peculiar, being as a rule polypoid tumours situated in the nasopharynx, larynx, trachea or intestines (22, 30) and sometimes recurring with many years' interval. Now and then they also occur as a kind of polyposis, especially when

situated in the intestines (11, 44, 58). Histologically they show typical plasma cells with no or very few mitotic figures.

The remaining plasmocytomas (55 %) are more or less malignant. The moderately malignant ones (c. 30 %) show a diffuse infiltrating, invading and now and then destructive growth, but usually they remain rather localized and solitary or involve the regional lymph nodes only and are accessible to surgical or radiological therapy. The microscopic picture shows somewhat atypical and polymorphous plasma cells, some mitoses, cells with 2—3 nuclei and now and then some monstrous polynucleated giant cells (25, 43, 46). Sometimes however these tumours can not be distinguished macroscopically or microscopically from the benign plasmocytomas, but the course and perhaps the microscopic picture of the metastases show their malignancy (20, 46).

The highly malignant extramedullary plasmocytomas are usually poorly demarcated, wide-spread, destructing and invading tumours or infiltrates, most frequently showing the picture of very malignant, expansive and destructing maxillary tumours (only 2 cases have been reported which were not localized within the upper air passages) that are almost intractable and very soon kill the patient. In the histologic picture are seen highly atypical and polymorphous plasma cells, many mitoses, many polynuclear and monstrous giant cells.

As mentioned above their first secondaries are in the regional lymph nodes, but sometimes bone metastases too are found at an early stage; however some cases have been reported with a very long interval before the manifestation of bone metastases, so by JACKSON, PARKER and BETHEA $8^1/_2$ years, PINEY and RIACH 12 years, JAEGER 16 years. The bony lesions which can not be distinguished roentgenologically from those of multiple myeloma are in both diseases localized to skull, vertebrae, costae, humeri and femora, while metastases distal to the elbow and knee joints are rare findings (25, 47).

The chemistry and histology of the blood have only been investigated in a few of the reported cases. The precipitation rate was followed by BING, JAEGER and RINGERTZ who find a normal or only slightly increased precipitation rate in patients with non-metastasizing plasmocytomas, but a significant increase when bone metastases had developed. Differential counts of the white blood corpuscles have only been made by few authors: MILIAN found in one case 2 % plasma cells but normal figures in the remaining patients; BASSET and SCAPIER too found a few plasma cells while the remaining authors have reported normal findings (20, 26, 53).

Bence-Jones protein could not be demonstrated by FIGI, BRODERS and HAVEN, GORMSEN or JAEGER, but in some cases which had de-

veloped bone metastases the Bence-Jones protein was demonstrated (17, 25).

The sternal marrow has been examined by some authors (6, 17, 20) but only in one case (17) an increased number of normal plasma cells was found, but no myeloma cells or other pathologic components.

Treatment and Prognosis

Most cases have been treated by surgery, sometimes followed by radiotherapy, and especially interstitial radium therapy with radium needles seems to be of value (17). However, still only a few cases have been reported (2, 3, 13, 17, 46, 55) with the patient living 5 years or more without signs of recurrence after a histologically verified malignant extramedullary plasmocytoma. Local recurrence has been noticed more than 9 years after the extirpation of the primary tumour (26), and also the benign, multiple plasmocytomas have a very great tendency at recurring locally (22, 49, 55, 57). The difficulty of making a clinical diagnosis and prognosis in these tumours is well illustrated in the cases reported by JACKSON, PARKER & BETHEA, PINEY and RIACH, RINGERTZ and other authors, in which the primary tumour either disappeared completely or remained stationary for many years after therapeutic measures, with bone metastases then suddenly becoming manifest and a very rapidly fatal course. So, excluding the conjunctiva plasmocytomas, the prognosis must be regarded as rather bad, which has also been stressed by some authors (f. e. 17), especially as the microscopic picture not always is in accordance with the clinical course, being sometimes benign with typical, uniform structure although the clinical progress of the disease is very malignant (46), and therefore these tumours must always be regarded and treated as being very malignant.

Case Reports

During the last 6 years 8 cases of plasmocytoma with extramedullary localization have been treated at the Radium Centre Aarhus, Denmark. Every case has been verified histologically.

Case 1. Patient 1401/43, a woman aged 73 was admitted with a plasmocytoma of the septum nasi after having suffered from intermittent epistaxis for 3 months and increasing wryness of the nose for about 2 months. No other symptoms had been noticed and the past history was uneventful. On admission a very considerable, neoplastic thickening of the septum was seen filling the whole left half of the nose and pressing the septum towards the right side. No involvement of the regional lymph nodes was found. Roentgenograms of skull, lungs and vertebral column: no abnormality, especially no signs of multiple myeloma. Laboratory data: No Bence-Jones protein was found. The sediment-

ion rate varied between 14 and 27 mm. White blood cell counts: normal figures. Differential counts: normal figures. Biopsy showed a malignant plasmocytoma. The patient was treated with roentgen rays 8,250 r (180 kv) during the following 2 months without any noticeable effect on the size of the tumour. Half a year later when the tumour was still unchanged, Radium 400 mch was given. 14 months later the tumour was still unchanged and a new biopsy showed again malignant plasmocytoma. As the patient was in good condition and no generalization could be demonstrated, Radium was tried once more, this time 360 mch. Now the tumour began decreasing and as a new biopsy 9 months later still showed plasmocytoma, a third Radium treatment of 150 mch was given. 4 months later the tumour had completely disappeared and now the patient has been without recurrence for 4 years.

Case 2. 1182/43, a foreman aged 39 had for 2 years had a sensation of a lump in the nasopharynx, snoring and secretion from the nose. A diagnosis of a malignant plasmocytoma rhino-pharyngis was made at another hospital and he was treated with roentgen rays, 6,050 r. After being well for about a year the patient was admitted here with a recurrence filling the right side of the pharynx and nasopharynx and with involvement of the retro- and parapharyngeal lymph nodes. Laboratory data: Sedimentation rate: 35 mm. White blood counts and smears: normal findings. Urinalysis: no Bence-Jones protein. Roentgenograms: destruction of the wall of the right maxillary sinus, but no signs of multiple myeloma. The patient was treated with roentgen rays for 3 weeks, then suddenly dies. Autopsy showed the malignant tumour and its metastases to the regional lymph nodes, but no distant lesions.

Case 3. 1278/44, a man aged 72 had a polyp removed from the nasopharynx after having had various vague sensations for 9 months. Microscopy showed malignant plasmocytoma. On admission at posterior rhinoscopy 3 more polyps of pea-size and a little ulcer were seen in the nasopharynx, but there was no involvement of regional lymph nodes. Laboratory data: Sedimentation rate 7 mm. Wassermann test negative. Blood counts and sternal marrow: no signs of myelomatosis. Roentgenograms showed normal findings. Roentgen treatment was given directed towards the nasopharynx, 3,680 r from each side, and when dismissed 8 weeks later no trace of tumour was detectable. The patient is still alive without recurrence or any other symptoms, now more than 5 years later.

Case 4. 953/43, a 77 years old widow was admitted with a plasmocytoma in the rhinopharynx after having for about 1 year increasing to complete nasal stenosis, headache in the forehead, giddiness and difficulty of hearing. Both nares were found to be completely occluded by tumour tissue and this was also found on the back wall of the rhinopharynx on digital exploration. Laboratory findings: proteinuria, but no trace of Bence-Jones protein. Negative Wassermann test. Precipitation rate 28 mm. Roentgenograms: skull: no destruction of the paranasal sinuses; lungs: no metastases. In the left submaxillary region a lymph node the size of a pea was found, but no other signs of metastasizing. However the patient was very weak and the course was constantly downhill and the patient died 7 months later although roentgen treatment was tried.

Case 5. 3557/47, a joiner aged 57 who had for $^1/_2$ year had a sensation of a lump in his pharynx noticed a little tumour behind the uvula and had it removed surgically. Histologic examination of the tumour, which was the size of a nut, showed plasmocytoma. On admission here no remnants were found and no involvement of the nodes in the neck. Roentgenograms and laboratory findings did not show any abnormality. Roentgen treatment was given, 9,460 r through 2 fields during 50 days, and now the patient has been well for more than 2 years without signs of recurrence.

Case 6. 713/45, a married woman aged 52 was admitted with a tumour of walnut size in the left submaxillary region which had been present for at least 2 years. The tumour was very firm, almost immobile, lying close to the mandible. No other tumours or palpable nodes were found. On admission a recently acquired syphilis was found and the patient was referred to a venereologic department for treatment. $^1/_2$ year later the tumour had increased to the size of a tennis ball. Puncture and biopsy showed plasmocytoma, so a preoperative roentgen treatment of 3,990 r was given. The tumour decreased considerably and was removed without difficulty. Laboratory findings: Sedimentation rate 30 mm, falling to 7 mm. Blood counts and sternal marrow: no sign of myelomatosis. Urine: no Bence-Jones protein. Roentgenograms: normal findings. Now $3^1/_2$ years after the operation the patient is still alive without recurrence or metastases.

Case 7. 221/46, a 34-year-old secretary was admitted with a history of increasing contact-bleeding at intercourse for c. 2 months. A characteristic cancerous, nodular tumour ulcer was seen in the right half of the portio, involving the right lacunar and vaginal wall, surrounded by a 2—3 mm high prominent edge. On digital examination the right parametrium was infiltrated. Biopsy showed plasmocytoma. All tests for venereal diseases were negative, and the laboratory findings (blood counts, urinalysis etc.) were all normal. She was treated with Radium, 3,600 mch twice with 10 days interval, and roentgen rays, totaling 9,400 r to 5 fields during 6 weeks. The patient is still alive and well $3^1/_2$ years after the treatment. On digital examination small, decreasing remnants of the infiltration felt in the right parametrium on the admission are still present.

Case 8. 2097/49, a merchant aged 72 had a growing right testis for about 2 months; then when it had reached the size of an orange he had it removed surgically. Histologic examination revealed a malignant, polymorphous-cellular plasmocytoma. No involvement of the regional lymph nodes was found. Intravenous pyelography showed normal conditions on the left side, but considerably delayed excretion in the right pelvis, and 5 weeks later no excretion at all. Roentgenograms of lungs, stomach, duodenum and pelvis: normal findings. Laboratory data: Sedimentation rate increasing from 40 to 52 mm. Hemoglobin from 75 % to 80 %. Wassermann test negative. Sternal marrow and blood counts gave normal figures. No Bence-Jones protein. The patient was treated with roentgen rays, 9,600 r through 8 ports towards the abdominal and mediastinal lymph nodes and is still alive.

Discussion. 8 cases, 4 female and 4 male, of extramedullary plasmocytomas have been presented. In 5 cases the tumour was situated in the upper air passages in accordance with this being the site of predilection of these tumours and in one case the tumour was in the submaxillary region. The last 2 cases were situated in the cervix uteri and the testis, localizations which have not been reported yet in the literature on plasmocytomas.

One case (no. 6) was complicated by a recently acquired syphilis. Although it is well-known that syphilitic lesions in skin and mucosal surfaces almost always show a great abundance of plasma cells, this can hardly be of any significance in this case in which the tumour had been manifest for 2 years before the syphilitic infection and in which the tumour was not affected by a very intensive antisyphilitic therapy — on the contrary it increased rather considerably in size. So one has no

reason to believe that this case was a case of inflammatory plasmocytoma. Case 3 was probably a case of multiple benign plasmocytomas while the remaining cases have been typical malignant extramedullary plasmocytomas of which 2 cases have progressed to death, giving a mortality of only 25 % at present. One patient has been without symptoms for more than 5 years and 4 patients for more than 3 years.

SUMMARY

The author gives a survey of the extramedullary plasmocytomas and reports a series of 8 cases, of which 5 were situated in the upper air passages, 1 in the submaxillary region and 2 in the genitals. At present 6 patients treated radiologically are alive and well, one patient living more than 5 years without recurrence or metastases.

ZUSAMMENFASSUNG

Der Verfasser gibt eine Übersicht über die extramedullären Plasmocytome und teilt eine Reihe von 8 Fällen mit, von welchen 5 in den oberen Luftwegen, 1 in der Regio submaxillaris und 2 im Gebiete der Geschlechtsorgane lokalisiert waren. Nach radiologischer Behandlung leben heute 6 Patienten, von denen einer seit mehr als 5 Jahren ohne Rezidiv oder Metastasen ist.

RÉSUMÉ

Après un aperçu des plasmomes extra-osseuses l'auteur rend compte d'une série de 8 cas, dont cinq etaient situés dans le nez et le rhino-pharynx, un cas dans la région sousmaxillaire et deux cas dans les organes génitaux. Après radiothérapie six de ces malades sont encore en vie et l'un d'eux n'a pas de récidive ou de metastases depuis plus de 5 ans.

REFERENCES

1) Adair, F. E.: Arch. Surg. vol. 26: 735: 1933.
2) Aragona, P.: Am. J. Cancer, vol. 32: 590: 1938.
3) Baldenweck, Z. and N. Perrot: Rev. de Laryng., vol. 59: 1267: 1933.
4) Basset, A. and I. Scapier: Monde méd., Paris, vol. 47: 7: 1937.
5) Bichel, J. and P. Kirketerp: Acta radiol., vol. 19: 487: 1938.
6) Bing, J.: Acta med. scand., vol. 91: 336: 1937.
7) — Acta med. scand., vol. 103: 547: 1940.
8) Blalock, J. W. S. and C. Macartney: J. Path. and Bact., vol. 35: 69: 1932.
9) Boit, H.: Frankf. Zeitschr. f. Path., vol. 1: 172: 1907.
10) Boyd, W.: Textbook of Pathology, 1938.
11) Brown, C. R. and A. F. Liber: Arch. Path., vol. 28: 112: 1939.
12) Carballo, R.: Folia haemat., vol. 43: 272: 1931.
13) Ciaccio, H.: Zentralbl. f. allg. Path. u. path. Anat., vol. 24: 104: 1913.
14) Cutler, C. W.: Am. J. Cancer, vol. 100: 393: 1934.
15) Cutler, M.: J. A. M. A., vol. 101: 1217: 1933.
16) Ewing, H.: Neoplastic diseases, 1942.
17) Figi, F. A., A. C. Broders and F. Z. Havens: Ann. Otol., Rhin. and Laryng., vol. 54: 283: 1945.

18) Fleischhaker, H. and R. Klima: Fol. haemat., vol. 56: 5: 1936.
19) — and — Münch. med. Woch., vol. 83: 2051: 1936.
20) Gormsen, H.: Knoglemarvsundersøgelser, Disp., København 1942.
21) Gronwald, G.: Zentralbl. f. Chir., vol. 58: 663: 1931.
22) Heindl, A.: Monatschr. f. Ohrenheilk. vol. 67: 878: 1933.
23) Hellwig, C. A.: Arch. Path., vol. 36: 95: 1943.
24) Hertz, R. and A. Mamrot: Fol. haemat., vol. 16: 227: 1913.
25) Jackson, H., F. Parker and J. M. Bethea: Am. J. Med. Sc., vol. 181: 169: 1931.
26) Jaeger, E.: Zeitschr. f. Krebsf., vol. 52: 349: 1942.
27) Jaffé, R. H.: J. A. M. A., vol. 107: 124: 1936.
28) James, W. M.: Am. J. Ophthalm., vol. 12: 731: 1929.
29) Kauffmann, E.: Lehrbuch d. spez. Pat. Anat., 1931.
30) Kreibig, W.: Arch. f. Ophthalm., vol. 131: 89: 1934.
31) Kusunoki, M. and A. Frank: Virchows Arch., vol. 212: 391: 1913.
32) Maresch, R.: Verh. d. deutsch. path. Gesellsch., vol. 13: 257: 1909.
33) Mattick, W. L. and A. A. Thibaudeau: Am. J. Cancer, vol. 23: 513: 1935.
34) McNamara, W. L. and R. J. Rogers: Arch. Path., vol. 36: 89: 1943.
35) Menzel, K. M.: Schweiz. med. Woch., vol. 71: 758: 1941.
36) Milian, G.: Bull. et mém. Soc. méd. hôp. Paris, vol. 55: 908: 1939.
37) Miller, J. K.: Am. J. Surg., vol. 43: 788: 1939.
38) Molotkoff, W. G.: Frankf. Zeitschr. f. Path., vol. 43: 508: 1932.
39) Montpelier, A., Choussat and Seurat: cit. after Gormsen, H.
40) Nordenson, N. G.: Acta path. and microbiol. scand., vol. 15: 362: 1938.
41) Papolczy, F. V.: Klin. Monatsbl. f. Augenheilk., vol. 83: 788: 1929.
42) Patek, A. J. and W. B. Castle: Am. J. Med. Sc., vol. 191: 788: 1936.
43) Piney, A. and J. S. Riach: Fol. haemat., vol. 46: 37: 1932.
44) Quensel, U.: Acta med. scand., vol. 68: 427 & 458: 1928.
45) Reiter, B. R. and J. T. Freeman: Am. J. Med. Sc., vol. 193: 38: 1937.
46) Ringertz, N.: Acta otolaryng., suppl. 27: 1938.
47) Rodman, J. S. and H. Ingleby: Ann. Surg., vol. 109: 921: 1939.
48) Rollin, J. L.: Zeitschr. f. Augenheilk., vol. 93: 181: 1937.
49) Rosenwasser, H.: Laryngoscope, vol. 40: 576: 1930.
50) — Laryngoscope, vol. 44: 826: 1934.
51) Roussy, G., R. Leroux and Ch. Oberling: Précis d'anat. path., 1942.
52) Schridde, H.: Zentralbl. f. allg. Path., vol. 16: 432: 1905.
53) Schwander, H., J. Estes and W. G. Cooper: Am. J. Path., vol. 23: 237: 1947.
54) Stancil, J. R. and W. J. Tomlinson: Arch. Otolaryng., vol. 40: 1939: 1944.
55) Stewart, M. J. and A. L. Taylor: J. Path. and Bact., vol. 35: 541: 1932.
56) Stout, A. P. and F. R. Kenney: Cancer, vol. 2: 261: 1949.
57) Tajkef, L.: Ann. d'oculist., vol. 171: 934: 1934.
58) Unna, P. G.: Monatschr. f. prakt. Dermat., vol. 12: 296: 1891.
59) Vasiliu, T. and R. Popa: Compt. rend. Soc. biol., vol. 98: 738: 1928.
60) Vogt, R.: Frankf. Zeitschr. f. Path., vol. 10: 129: 1912.
61) Wachter, H.: Arch. f. Laryng. u. Rhin., vol. 28: 69: 1913.
62) Waltner, J. G.: Ann. Otol., Rhin. and Laryng., vol. 56: 911: 1947.
63) Willis, R. A.: Pathology of Tumours, London 1948.

FROM THE RADIOLOGICAL DEPARTMENT OF THE UNIVERSITY HOSPITAL, COPENHAGEN, DENMARK (CHIEF: PROFESSOR P. FLEMMING MØLLER, M. D.)

PHLEBOGRAPHY IN CHRONIC VENOUS INSUFFICIENCY OF THE LOWER EXTREMITY[1]

A Preliminary Report

by

I. C. Højensgård

The object of this paper is to contribute to elucidating the practical significance of phlebography in the treatment of chronic venous insufficiency of the lower extremities. The author has had no experience in the phlebographic diagnosis of acute thrombosis, and he is therefore not prepared to say whether the technique described below is suitable for this end.

First a brief description will be given of the pathological anatomy and physiology of chronic venous insufficiency on the basis of recent investigations. The term »chronic venous insufficiency» is taken to mean all chronic conditions in which the venous return is impaired because of destruction of the venous-muscular pump mechanism. By far the most important ones are (1) primary or idiopathic varicosities (insufficiency of the superficial venous system), and (2) postthrombotic conditions (insufficiency of the deep venous system).

Postthrombotic conditions: When acute thrombosis of the deep veins of the lower extremity occurs, these veins will become blocked, and a collateral circulation will soon be established in the superficial veins. This collateral circulation, which has been elucidated particularly by BAUER (1942), is more or less effective in the return flow of venous blood from the lower limb. When the acute stage of the thrombosis has passed, the patient may in a few cases be practically symptomless for the rest of his life. In the great majority of cases, however, it will be followed — perhaps after a few years' symptomless interval — by a more or less disabling condition (involving varicosities, oedema, induration, eczema, ulcer,

[1] Read before the Danish Radiological Society, Jan. 19, 1949; submitted for publication, Aug. 20, 1949.

sensations of heaviness and fatigue, as well as pain). The development of these sequelæ from the state of acute thrombosis has been emphasized first by BAUER (1942). They are usually progressive and arise, according to BAUER, because the collateral circulation in the superficial veins, which at the outset is functionally sufficient, now degenerates (with development of valvular incompetence and varicosities), while the deep veins remain obliterated. Others again (BUXTON and COLLER 1945, HOMANS 1946, LINTON and HARDY 1948) suppose that the postthrombotic sequelæ are caused by recanalization of the deep veins, resulting in irregular venous lumina with destroyed valves allowing a reversed blood flow. Presumably both changes (and perhaps even other factors) are of significance. There is a predominant likelihood that this lack of functioning valves in the principal veins is the fundamental pathogenetic factor in postthrombotic chronic venous insufficiency, as active transport of blood in the proximal direction is impossible, if the veins are valveless. This is also apparent from the fact that exercise (*e. g.* walking) with compression of incompetent superficial veins does not produce a fall in the venous pressure in the legs of patients suffering from postthrombotic conditions as it does in patients with primary varicosities (HØJENSGÅRD and STÜRUP 1949).

Primary varicosities: Unlike postthrombotic conditions with ineffective *deep* veins (due to obliteration or valvular incompetence), an ordinary, primary, varicose state shows effective deep veins. In the latter condition the pathological feature is incompetence or absence of valves in the important *superficial* veins (the great or small saphenous vein). If these insufficient venous trunks are compressed, extirpated or obliterated, so that reversed flow of blood is prevented, normal physiological conditions are re-established as far as the transport of the blood into the proximal direction is concerned, and muscular activity will cause a fall in the venous pressure in the leg (HØJENSGÅRD and STÜRUP 1949).

According to certain authors (MARTORELL 1946, BAUER 1948) the state of lacking or insufficient valves in the deep veins may occur unpreceded by thrombosis (BAUER: idiopathic deep venous incompetence). It has been demonstrated by BAUER that contrast medium injected into the distal direction into the femoral vein in the inguen will travel down into the femoral vein, popliteal vein, and even into the deep veins of the leg in certain patients affected with primary varicosities just as in patients with postthrombotic recanalized deep veins, whereas it will be arrested by valves a few centimetres below the site of the injection in the majority of patients with primary varicose veins (as in normal subjects). As regards the function of the veins, this condition is, according to BAUER, analogous to that of postthrombotic insufficiency.

Other workers (LUKE 1943, SANDEGÅRD 1949), using the same technique, have, however, failed to demonstrate this particular group of patients with primary varicosities. They report that even in normal subjects, the dye may travel far distally through the deep veins and therefore think that it does pass normally functioning valves.

The treatment of *primary varicosities* with sufficient valves in the deep veins is simple and well-known: The most common procedure is ligation of the incompetent superficial venous trunk proximally where it joins the femoral vein (insufficiency of the great saphenous vein) or the popliteal vein (insufficiency of the small saphenous vein) combined with extirpation or chemical obliteration of the entire varicose area.

The treatment of the *postthrombotic condition* has always been unsatisfactory. Bandaging (according to the technique of BISGAARD 1939, or BIRGER 1947, or similar methods) appears to be most effective. During recent years a method which formerly was used to some extent by a few, particularly French, surgeons has been revived, *i. e.* ligation of the insufficient recanalized deep vein, either the femoral vein (BUXTON and COLLER 1945, HOMANS 1946, REES and SLEVIN 1947, LINTON and HARDY 1948, SANDEGÅRD 1949) or the popliteal vein (BAUER 1948). This method is based on the idea that in certain circumstances there may be a reversed blood flow in valveless deep veins in the same way as it is presumed to be in superficial varices. Ligation of the deep vein is supposed to prevent this distal flow and thus relieve the stasis in the leg. This treatment has also been employed by BAUER in those cases where he has diagnosed »idiopathic deep incompetence». — The method appears to be promising, but the cases treated are still too few to allow of any evaluation of its effectiveness.

Since clinical examination as well as past history may at times fail to decide whether a state of venous insufficiency is of primary or postthrombotic nature, and since the active therapy mentioned presupposes a knowledge of the state of the deep veins, phlebography may acquire a certain significance in this form of treatment. It helps to decide whether the deep veins are furnished with normal valves or whether they are recanalized and valveless, or whether there are any permeable deep veins at all or merely collaterals. It is difficult to arrive at such a decision using the ordinary phlebographic technique of examining the limb in the *horizontal* position, a technique which especially is unable to decide the most important question in this connection, *i. e.* whether there are valves or not in the deep veins. This is presumably the reason why earlier papers on phlebography have not emphasized this important detail. In the writer's experience this question can only be decided, if the limb is examined in the *vertical* position. The advantages of the latter technique are as follows:

(1) Owing to better filling of the veins in the vertical position and to the high specific gravity of the opaque medium (perabrodil etc.), the valvular sinus is visualized distinctly in this posture (as demonstrated by LINDBLOM in 1941 and KJELLBERG in 1943), showing maximum distention of the sinus and high intensity of the contrast. In the horizontal limb the

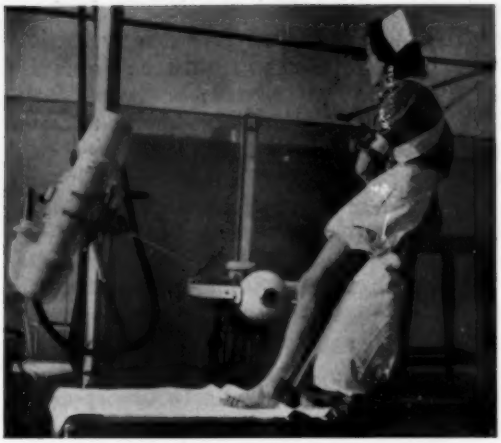


Fig. 1. The technique used (position of patient and tubes).

valvular sinus is not distended, and the contrast will not be particularly dense here. This is shown in Fig. 2. Phlebography of the horizontal limb involves the possibility of confusing a primary varicose state with normal deep veins and a postthrombotic state with recanalized deep veins.

(2) In the horizontal limb the posterior (*i. e.* the lowest) veins will fill more easily than the others due to the high specific gravity of the contrast medium (LINDBLOM 1941). Therefore one cannot be sure of obtaining filling of the deep veins proper which are situated more anteriorly. In postthrombotic limbs there will be numerous muscular and subcutaneous collaterals in the calf, and the heavy contrast medium will perhaps seek them out. LINDE (1949) has suggested that this might be the explanation why BAUER has maintained until quite recently, on the basis of phlebographic studies of horizontal extremities, that recanalization of deep thrombosed veins hardly ever occurs (BAUER 1942). In the vertical position there is not in that respect any reason to expect that the contrast medium should prefer certain paths to others. When using this technique, one will discover that the great majority of thrombosed deep veins are recanalized (according to LINDE 1949 at least 73 per cent., in the author's experience even more).

(3) In the horizontal limb the lateral views will show that the contrast medium may run along the posterior aspect (»bottom») of the major veins, so that it is difficult to form an opinion of the size and outlines of the vein (Figs. 3 and 4, see also LINDBLOM 1941 and KJELLBERG 1943). This phenomenon is of course not met with in a vertical limb.

(4) It has been emphasized by BAUER 1940 and FRIMANN-DAHL 1947 that in a leg resting on the couch there may easily be compression of the deep veins in their course through the calf, and that resulting filling defects are apt to be misinterpreted as obliteration of the venous lumen. This may, however, be prevented by supporting the heel so that the calf does not rest on the couch (BAUER 1940).

a.

b.

Fig. 2. Phlebography of a normal lower limb:
(*a*) in the vertical position (distinct valves),
(*b*) in the horizontal position (no valves visible).

(5) Lastly, phlebographic examination should be done with the leg in the vertical position for physiological reasons. From the point of view of pathology, it is immaterial through which venous pathways the blood flows in the horizontal position, as *chronic* venous insufficiency gives no symptoms at all in the horizontal position, but only in the erect posture where hydrostatic phenomena manifest themselves. In the horizontal position the venous system is always sufficient in such chronic diseases, even though the patients may experience serious symptoms of insufficiency when erect. This is due to the fact that the insufficiency is not as previously assumed caused by a diminished calibre of the entire venous system, resulting from the obliterative thrombotic process, but by non-functioning of the pump mechanism (because of incompetence of the valves in the superficial or deep veins). In this chronic condition the aggregate calibre of the venous lumina presumably is always sufficient to convey the necessary amount of blood because of the ample collaterals.

It has been stated (BAUER 1947) as an argument against the vertical position that fewer veins are visualized in the horizontal than in the vertical position in which muscular veins and subcutaneous veins will stand out nearly as distinctly as the deep pathways which are the objects of the study. Filling of the subcutaneous veins can, however, be prevented by compression (*vide infra*), and with some experience the interpretation is always possible when phlebograms are made in two planes. — The

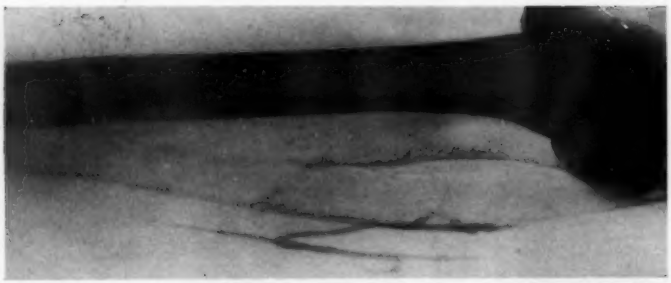


Fig. 3.

Fig. 4.

Fig. 3. The limb in the horizontal position. The opaque medium seeks out the lowest veins.

Fig. 4. Horizontal position. Opaque medium confined to the »bottom» of the vein.

intensity of the contrast is perhaps somewhat fainter in a vertical than in a horizontal limb as the limb contains more blood in the former position. This difference is, however, eliminated to some extent by the more rapid flow of blood in the horizontal position, and if the exposure is timed correctly, phlebography of a vertical limb is rarely unsuccessful on account of a too faint contrast. — On the whole, these two objections do not amount to much as compared with the advantage of vertical above horizontal positioning, *i. e.* that the fundamental question as to the presence or absence of valves in the deep veins can be answered only by application of the vertical position.

Technique

The technique of vertical positioning was suggested by LINDBLOM in 1941 and has been employed particularly by LÖFSTEDT (1946). The method used by the author is that of LÖFSTEDT with only a few minor modifications.

The patient sits on a high chair or stool (Fig. 1), the leg to be examined hanging down. Two views are made: an *antero-posterior* (*i. e.* with about

30° internal rotation of the leg to make the space between the tibia and fibula widest possible) and a *lateral* one (with 10—15° internal rotation of the leg). At least 2 exposures should be made in each view, because there are great individual variations in the rate of the blood flow which is most rapid in normal, and slowest in postthrombotic subjects. The following exposures are suggested:

1st exposure: antero-posterior
2nd exposure: lateral

These two views comprise the leg and the region of the knee joint.

3rd exposure: antero-posterior
4th exposure: lateral

In the two latter views the cassette is placed slightly more proximal, in order that as large a part of the thigh as possible be included without moving the tubes which are centred immediately below the knee. — The film size is 15 × 40 cm. The cassette for the antero-posterior exposure is supported by a firm pillow behind the almost vertical leg (which of course must not *rest* on the pillow), and the other one is held in the hand against the lateral aspect of the leg.

In order to prevent the dye from selecting the superficial veins, it is usually necessary to tie a tourniquet firmly around the malleolar region, and in the presence of varicosities an elastic bandage must be wound around the leg after it has been emptied of blood by elevation. Occasionally it may be desirable to place a tourniquet immediately below the knee (*vide infra*), a procedure which must be recommended in every case with a past history of definite or suspected thrombosis.

The contrast media used are perabrodil, uriodone, diodrast, or similar preparations, 35 or 50 per cent. The injection is always painless. Occasionally it is followed by some nausea, but more rarely than one would expect in view of the comparatively rapid injection and considering that the patients are sitting or almost standing. This is presumably due to the slow flow of blood in the vertical, resting position and to the admixture of a large amount of blood. The injection is made with an ordinary hypodermic needle, percutaneously, as a rule into a vein on the dorso-median aspect of the base of the great toe. A total of 20 ml. is injected as quickly as possibly (in less than one minute). It is important not to make the exposures too soon. Fifteen seconds should lapse from the injection has been completed until the 1st exposure is made, and then the other exposures are made at 10—20 seconds' intervals. In that way the last exposure takes place at least 1 and preferably 2 minutes after the injection has been completed. Care should be taken that the leg muscles are relaxed between the exposures so that the sedimentation of the opaque medium in the valvular sinus may take place undisturbed. Therefore, the radiologist

must rotate the patient's leg the 20—30° between the exposures and not leave this to the patient.

Several workers, *inter alia* BAUER, prefer exposure of the small saphenous vein behind the lateral malleolus and injection of the contrast medium into this site, where the vein has a constant and wide communication to the deep fibular vein which then will fill primarily. BAUER states, however, that as a rule he also obtains filling of the other deep leg veins which — in his words — are small and unimportant. Other workers complain of difficulty in obtaining filling of all the deep veins when the injection is made behind the lateral malleolus. Like LINDBLOM, LÖFSTEDT and most other authors, the writer prefers percutaneous injection into a distal vein of the foot. In favour of this method the following may be mentioned:

(1) In the retromalleolar region there are cutaneous lesions in numerous cases of primary varicosities and in nearly all instances of postthrombotic conditions (oedema, induration, eczema etc.). An incision at this site must involve the risk of infection and slow healing. According to BAUER (1945) this complication is, however, rare.

(2) In postthrombotic and varicose cases one should probably think twice before producing a scar in an area which is the site of predilection of chronic leg ulcer. BUXTON and COLLER 1945 and STÜRUP 1949 have called attention to the significance of scars in the ætiology of varicose and postthrombotic leg ulcer. When dealing with patients with a completely healthy skin, it should be borne in mind that they may acquire varices or thrombosis later.

(3) Lastly a physiologically more true picture of the venous return will probably be obtained, if the opaque medium is allowed to mix with the blood in a situation as peripheral as possible instead of introducing it directly into one of the principal draining veins of the leg.

Percutaneous injection is not difficult and requires much less time than exposure of the vein. Paravenous injection was followed by necrosis in one of the author's cases and should therefore be avoided.

Results

On the basis of a phlebographic study of more than 200 lower limbs affected with chronic venous insufficiency, and a number of normal legs, the following characteristics may be set up for the phlebographic findings in normal and pathological extremities:

Normal Lower Limbs. (Figs. 2 *a* and 5).

The antero-posterior view shows the deep crural veins in the space between the tibia and fibula. In the lateral view they are close to or partly hidden by the posterior aspect of these bones. The number and course of the veins are extremely varied. As a rule it is, however, possible to distinguish three veins: the anterior tibial, posterior tibial, and fibular veins. All of them may be single or double in their entire course or part thereof. — The popliteal and femoral veins run a characteristic course which must be noted (Fig. 5 *b*) as the great saphenous vein in pathological conditions may easily be mistaken for the popliteal or femoral vein in the lateral view. The femoral vein runs along the convex curve of the femoral

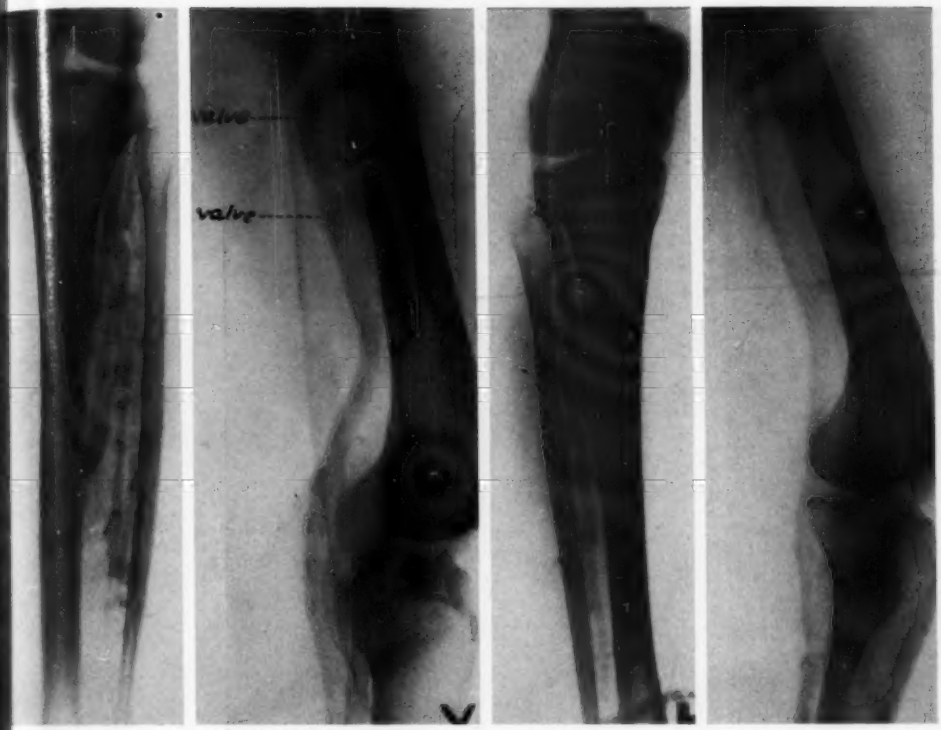


Fig. 5 *a*. Fig. 5 *b*. Fig. 6 *a*. Fig. 6 *b*.

Fig. 5. Normal limb, (*a*) antero-posterior, (*b*) lateral view. Note the course of the femoral vein and the great saphenous vein.

Fig. 6. Limb with small, primary varicose veins and ulcer of the leg. Normal deep veins, (*a*) antero-posterior, (*b*) lateral view.

condyles, and the concave curve of the popliteal space at a certain, short distance from the bone contour, whereas the great saphenous vein takes a more straight course. The outlines of the veins are fairly even and straight. — In the crural veins numerous valves are visible at intervals of 1 to a few cm. In the popliteal vein there are normally 2 or 3 valves. Fig. 5 *b* shows the characteristic localization of the two most distal valves of the femoral vein. — Apart from the deep veins only a few are visualized. At times the opaque medium is seen in occasional muscular and subcutaneous veins of fine calibre.

Fig. 7 *a*.

Fig. 7 *b*.

Fig. 8 *a*.

Fig. 8 *b*.

Fig. 7. Limb with primary varicose veins. Normal deep veins with muscular collaterals, (*a*) antero-posterior, (*b*) lateral view.

Fig. 8. Limb with primary varicose veins, induration, ulcer, and poor evacuation of the varicose veins in Perthes' test. Normal outlines and course of the deep veins, but few definite signs of valves, (*a*) and (*b*) antero-posterior views.

Lower Limbs with Primary Varicosities.

In most instances the deep veins look exactly like those in a normal limb (Figs. 6 and 7), but this is not always the case. There are, for instance, deep veins which are slightly dilated and with contours less even than those of the normal deep veins. Actual »deep varices» — a condition which is often presumed to exist — are never met with, if this is taken to mean considerably dilated and tortuous, valveless veins. In a few instances fewer valves are visible than in normal limbs (Fig. 8), and in ex-

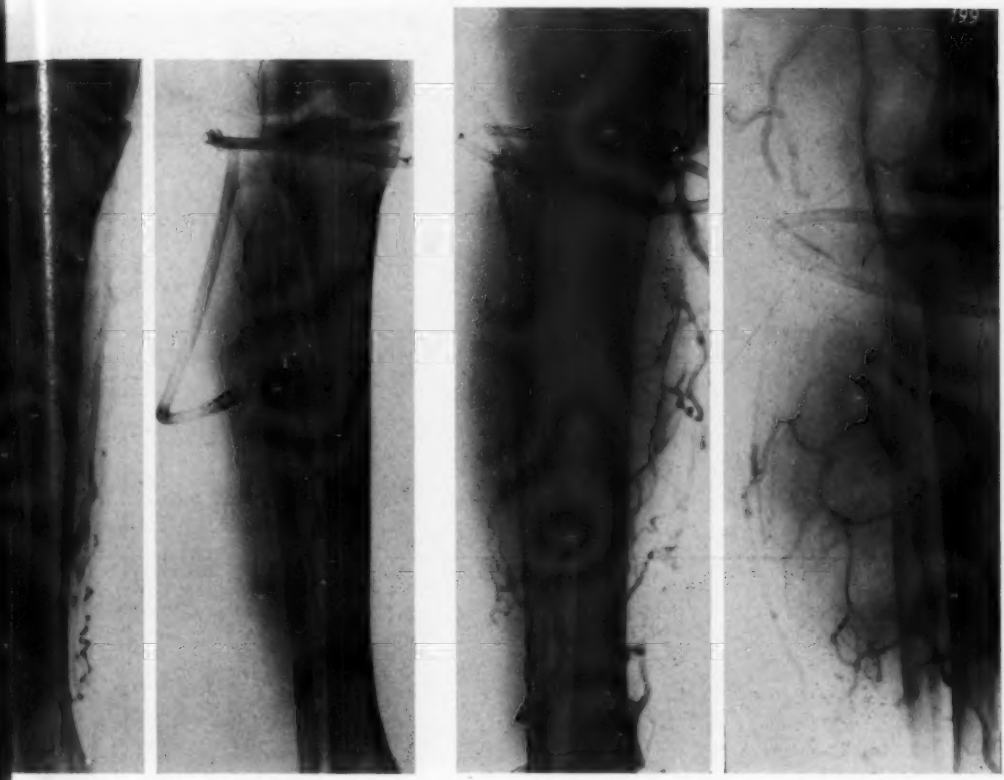


Fig 9 *a*. Fig. 9 *b*. Fig. 10 *a*. Fig. 10 *b*.

Fig. 9. Limb with postthrombotic varicose veins, induration, and ulcer. (*a*) without application of tourniquet (the opaque medium follows the great saphenous vein), (*b*) with tourniquet around the knee (the great saphenous vein is not visualized and the opaque medium is forced through recanalized, deep veins).

Fig. 10. History of thrombosis 22 years ago. The limb now shows secondary varicosities, oedema, but no ulcer. There is subjective discomfort. (*a*) anteroposterior, (*b*) lateral view. In spite of the tourniquet there is no opaque medium in the deep veins, but only in the subcutaneous ones, especially the great saphenous.

ceptional cases there are no definite signs of valves. The author does not know for certain whether this is due to failure of the phlebographic technique or to a real phenomenon. The former is more likely as these patients in the series under discussion exhibited evacuation of the varicose veins in Perthes' test, *i. e.* function of the deep veins. No instance of

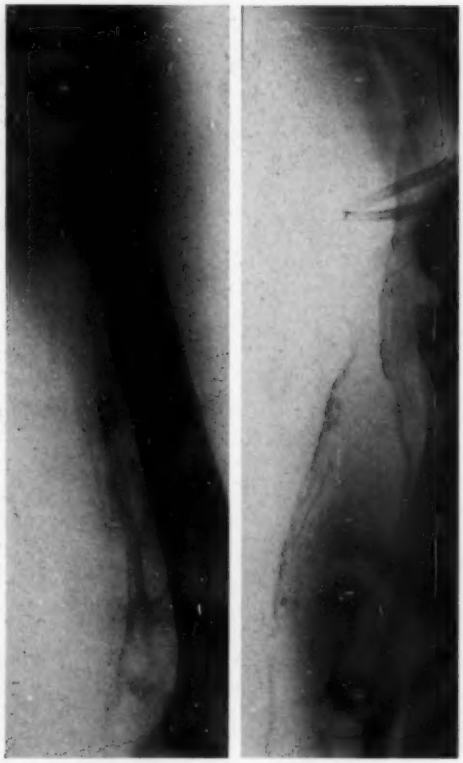


Fig. 11. Fig. 12.

Fig. 11. History of deep thrombosis 6 months ago. »Net-like» or spongy (= beginning) recanalization of the popliteal and femoral veins.
Fig. 12. History of deep thrombosis 1 year ago. »Net-like» recanalization of the deep veins.

definitely lacking valvular function of the crural deep veins occurred in the writer's series in cases where previous deep thrombosis could be ruled out with certainty. — Unlike normal lower limbs, limbs affected with primary varices usually exhibit the opaque medium in a number of superficial or muscular veins (Fig. 7).

Postthrombotic Lower Limbs.

The phlebographic appearance is extremely varied, depending *inter alia* on the technique and the interval from the acute thrombosis until

Fig. 13.

Fig. 14 *a*.

Fig. 14 *b*.

Fig. 13. History of deep thrombosis. Now, secondary varicose veins, oedema and subjective complaints, but no ulcer. A typical picture of recanalized deep veins and collaterals.

Fig. 14. History of deep thrombosis. Now, oedema, induration, and ulcer, but no varicosities. (*a*) antero-posterior, (*b*) lateral view. Recanalized deep veins with collaterals in the muscles and subcutaneous tissue.

the examination. At times no deep veins are seen. Experience indicates that as a rule this is due to failing technique. A tourniquet around the knee will in some cases force the blood into deep venous channels into which the blood would not otherwise find way (Fig. 9); in other instances the exposure may have been made at the wrong moment (usually too early so that a later film will show the opaque medium in the deep veins). There are probably, however, cases in which the deep veins are not permeable (Fig. 10); this applies at least during the time immediately

Fig. 15 *a*. Fig. 15 *b*. Fig. 16.

Fig. 15. History of deep thrombosis. Now, oedema and ulcer, but no varicosities. (*a*) antero-posterior, (*b*) lateral view. Sparse recanalization of the deep veins. Numerous deep and superficial collaterals filling although a tourniquet was placed around the knee.

Fig. 16. History of deep thrombosis. Now, ulcer and secondary varicose veins. Large, recanalized lumina in the deep veins, no collaterals.

after acute thrombosis. It appears, however, to be an extremely rare occurrence that the deep veins remain blocked, at any rate the popliteal and femoral veins. In that case the blood is conveyed by collaterals, mainly subcutaneous. — Shortly (*i. e.* a few months) after an attack of acute thrombosis the structure of the popliteal and femoral veins is »net-like» or spongy (Figs. 11 and 12), indicating beginning recanalization. — Later this pattern does not appear (Figs. 13—16). The lumen may now be of dimensions approximately normal or even larger, but somewhat

irregular and with outlines less even than in normal subjects. — The typical appearance of the crural veins is that of numerous, small, extremely uneven, tortuous, richly anastomosing veins, distinctly differing from that in normal subjects and patients with primary varicose veins. These irregular veins presumably represent recanalized deep veins as well as dilated preformed small veins (satellite veins, venae vasorum). In addition, there will always be major superficial or muscular collaterals. Filling of the superficial veins may, however, usually be prevented by tightening a tourniquet around the knee. Lastly, no valves are seen in the crural deep veins in postthrombotic extremities (at any rate not in those where the thrombosis must be presumed to have been total) and probably not either in the collaterals.

The characteristic features of the different varieties may be roughly tabulated as follows:

Deep veins of the leg:	In normal subjects	In cases of primary varicosities	In postthrombotic conditions
Course	Straight	Straight	Irregular, tortuous
Outlines	Even	Almost even	Irregular
Lumina	Regular	Fairly regular	Extremely irregular
Valves	Numerous	Numerous, usually distinct	None
Collaterals	None	A few	As a rule many

In a later paper the writer will deal in more detail with the material forming the basis of the experience related above.

SUMMARY

After describing the pathological features of chronic venous insufficiency (primary varicosities and postthrombotic conditions), emphasizing the state of the valves as the essential factor, the author describes a phlebographic technique applicable in such instances. It is stressed that the limb should be examined in the vertical position, as this will best ensure filling of the deep veins, and as the venous valves are visualized only in this position. Percutaneous injection of the opaque medium is preferred to exposure of a vein. The appearance of the deep veins in normal subjects, in patients with primary varicosities, and in patients with postthrombotic conditions is described and illustrated.

ZUSAMMENFASSUNG

Nach einer Besprechung der pathologischen Züge der chronischen Veneninsuffizienz (primäre Krampfadern und postthrombotische Zustände), wobei der Zustand der Klappen als ausschlaggebender Faktor hervorgehoben wird, beschreibt Verf. eine in solchen Fällen verwendbare phlebographische Technik. Es wird betont, dass die Extremität in senkrechter Stellung untersucht werden muss, da dies die Füllung der tiefen Venen am besten

gewährleistet, und da die Venenklappen nur in dieser Stellung sichtbar werden. Perkutane Einspritzung des Kontrastmittels wird der Blosslegung der Vene vorgezogen. Das Aussehen der tiefen Venen bei Gesunden, bei Kranken mit primären Krampfadern und bei Kranken mit postthrombotischen Zuständen wird beschrieben und veranschaulicht.

RÉSUMÉ

Après avoir brossé le tableau pathologique de l'insuffisance veineuse chronique (varicosités primitives et états postthrombosiques), en soulignant que l'état des valvules est le facteur essentiel, l'auteur décrit une technique de veinographie applicable à ces cas-là. Il insiste sur la nécessité d'examiner le membre en position verticale qui assure le mieux le remplissage des veines profondes, et parce que c'est seulement ainsi que les valvules sont rendues visibles. Il préfère l'injection transcutanée de la substance opacifiante à la mise à nu d'une veine. Il décrit, et illustre par des images, l'aspect des veines profondes chez des sujets normaux, chez des malades à varicosités primitives, et chez d'autres atteints de lésions postthrombosiques.

REFERENCES

Bauer, G.: Acta chir. Scand. *84:* suppl. 61, 1940.
— Acta chir. Scand. *86:* suppl. 74, 1942.
— Acta rad. *26:* 577, 1945.
— Sv. Läkartidn. *44:* 1757, 1947.
— Journ. internat. de Chir. *8:* 937, 1948.
Birger, I.: Acta chir. Scand. *96:* suppl. 129, 1947.
Bisgaard, H.: Ulcus og eczema cruris, Copenhagen 1939 (English translation, Copenhagen 1948).
Buxton, R. W. and F. A. Coller: Surgery *18:* 663, 1945.
Frimann-Dahl, J.: Acta rad. *28:* 199, 1947.
Homans, J.: New Engl. J. Med. *235:* 249, 1946.
Højensgård, I. C. and H. Stürup: Acta chir. Scand. *99:* 133, 1949.
Kjellberg, S. R.: Acta rad. *24:* 433, 1943.
Lindblom, K.: Acta rad. *22:* 288, 1941.
Linde, P.: Acta chir. Scand. *97:* 430, 1949.
Linton, R. R. and I. B. Hardy, Jr.: Surgery *24:* 452, 1948.
Löfstedt, S.: Nordisk Medicin *31:* 1535, 1946.
Luke, J. C.: Canad. Med. Ass. Journ. *49:* 86, 1943.
Martorell, F.: Varices. Su tratamiento basado en la flebografía. Madrid 1946.
Rees, H. C. and J. G. Slevin: Surgery *21:* 575, 1947.
Sandegård, E.: Nordisk Medicin *41:* 560, 1949.
Stürup, H.: Monograph (to be published).

FROM THE ROENTGEN DEPARTMENT OF THE HOSPITAL »CALVARIENBERG» AT MAASTRICHT, HOLLAND (CHIEF: DR. G. J. VAN DER PLAATS)

IS A ROENTGENOGRAM OF FINE STRUCTURES A SUMMATION IMAGE OR A REAL PICTURE?[1]

by

Dr. *J. E. J. Resink*, Rotterdam

When an accumulation of many small similar details are found in an object, apparently the roentgenogram only shows part of them. For instance, if we examine a roentgen picture of miliary tuberculosis of the lungs, it seems to the observer as if the photograph shows as many foci as there are on the section of the preparation. Several workers in this field of reserach have subjected this phenomenon to experimental examination. At first it was generally assumed that only the foci that were lying closest to the film appeared on the picture. No doubt this was so during the first decades of roentgen research, for the photographs then made (unsharp because of the large focus and taken at short distance, etc.) were not of a kind to bring out small details that were situated at some distance from the film but reproduced these either very vaguely or not at all. Other workers thought that the image produced was a summation image, however. It was chiefly due to FRANKE that this summation theory became fairly generally accepted. According to this view of the matter the foci appearing on the photograph are not pictures of certain elements in the object but are the result of the superposition of the shadows of many foci situated one behind the other. The assumption is that the individual foci cannot be made to show on the picture independently, and according to the supporters of this theory the above applies to all roentgenograms of all objects in which many similar details are accumulated, such as bone, miliary pulmonary tuberculosis, the network of the lungs and a gall-bladder containing a large number of stones. The summation theory supposes that roentgenograms of these objects produce images due to superposition, a striking feature of which is the resemblance shown between the images and the elements constituting the object.

[1] Submitted for publication, June 20, 1949.

In 1942 CHANTRAINE called this theory in question. In his opinion the images obtained are real images, or in other words the details appearing on the roentgenogram represent definite details in the object. He based his views chiefly on stereoscopic observations. He declared that the above-mentioned details (trabeculae, miliary foci, etc.) are visible in space on stereoscopic pictures and must therefore be pictures of individual elements. FRANKE's comment on this view was that the images observed by CHANTRAINE are not real three-dimensional pictures but fictitious ones.

The discussion that developed between FRANKE and CHANTRAINE inspired the present writer to undertake further research in connection with this question. The object of his investigations was, therefore, to determine whether roentgenograms of fine structures are summation images or real ones. Obviously, experimental investigation of a problem of this kind involves the use of objects that present these fine structures on the roentgenogram. This suggests the employment of anatomical preparations, care being taken that all conditions that might in any way affect image forming remain as nearly as possible the same as in the case of the living organism. It is possible, however, to make experiments with non-anatomical phantoms, but these have one disadvantage, namely, that their details and structure resemble very little those of the organs that produce the above-mentioned roentgenogram, so that results obtained from them cannot be directly applied to the latter. On the other hand they have advantages too, in that certain factors (details that are equal or unequal in size, regularly or irregularly distributed, etc.) can be arranged as circumstances demand and hence their influence on the forming of images can be studied. Furthermore, one knows more of the build and structure of the objects than in the case of anatomical test objects. All this makes it possible to form rules or laws that are generally applicable and therefore also applicable to roentgenograms of living organs. For this reason the experiments described in the present paper were made with both non-anatomical phantoms and anatomical preparations.

A. Research with Non-Anatomical Phantoms

In the case of objects that show a fine structure on the roentgenogram (such as miliary foci, trabeculae, etc.) we were dealing with an accumulation of many, small details that greatly resemble one another. According to the summation theory the roentgen picture of structures of this kind is formed by the superposition of the »shadows» of the elements constituting the object, while the separate details themselves do not appear as such on the photograph. If, however, we assume that the

Fig. 1 a.

Fig. 1 b.

a. Fourteen cards showing irregularly distributed holes 7 mm in diameter. These remained on the film during the whole period of exposure. The holes were strongly supraliminary.

b. The same cards. This time they had been left on the film for only 1/4 of the total period of exposure. The holes were just infraliminary. No images due to summation appeared.

details observable on the photograph are pictures of distinct elements in the object, then such elements are individually visible on the roentgenogram. Hence it is evident that in studying this problem a clear distinction must be made between details that are not separately represented in the picture (known as infraliminary details) and details which do appear separately (known as supraliminary details).

It is a great pity that this point was not sufficiently borne in mind in connection with the experiments that led to the forming of the summation theory — the well-known tests made by FRANKE with peas, for instance. The elements in these were mostly strongly supraliminary. Furthermore, in all these experiments the elements were exactly similar and often very regularly distributed which is generally not the case in the human body.

It was, however, very difficult, technically, to find objects that were just infraliminary or just supraliminary. We therefore adopted a method suggested by CHANTRAINE. If a test object is left on the film for only part of the time of exposure, while the film alone is exposed for the rest of the period, the same effect is produced as when a thinner object of the same kind is left on the film during the entire period of exposure. Now if we gradually reduce the fraction of the whole period of exposure

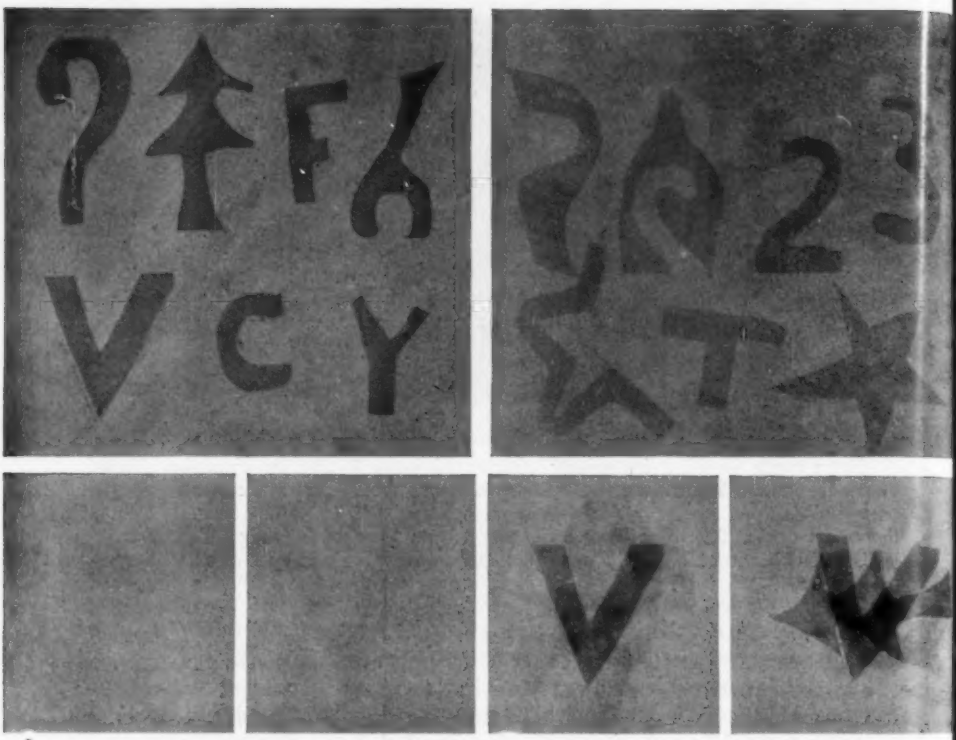


Fig. 2. These photographs show (a) seven bits of wood 5 mm thick; (b) seven bits of wood 2.3 mm thick; (c) six bits of wood 2.3 mm thick placed one above the other; the blocks were just infraliminary; (d) six blocks 2.3 mm thick (just infraliminary) and one 5 mm thick (just supraliminary). On the original photograph one V-shaped bit of wood is just recognizable. (e) Six blocks 2.3 mm thick and one 5 mm thick superposed and all supraliminary. (f) Six blocks 2.3 mm thick and two 5 mm thick superposed and all supraliminary.

during which the element is allowed to remain on the film, the contrast between the rays gets less and less, until finally it is so small that it makes no distinguishable contrast on the film. In this way the threshold of visible contrast may be easily determined, after which it becomes a simple matter to choose a contrast that will be just distinguishable or not on the film and is hence either just infraliminary or supraliminary.

Naturally care had to be taken to insure there being the same conditions when a single layer of elements was photographed as when there were several layers, so that there might be no technical reason why in

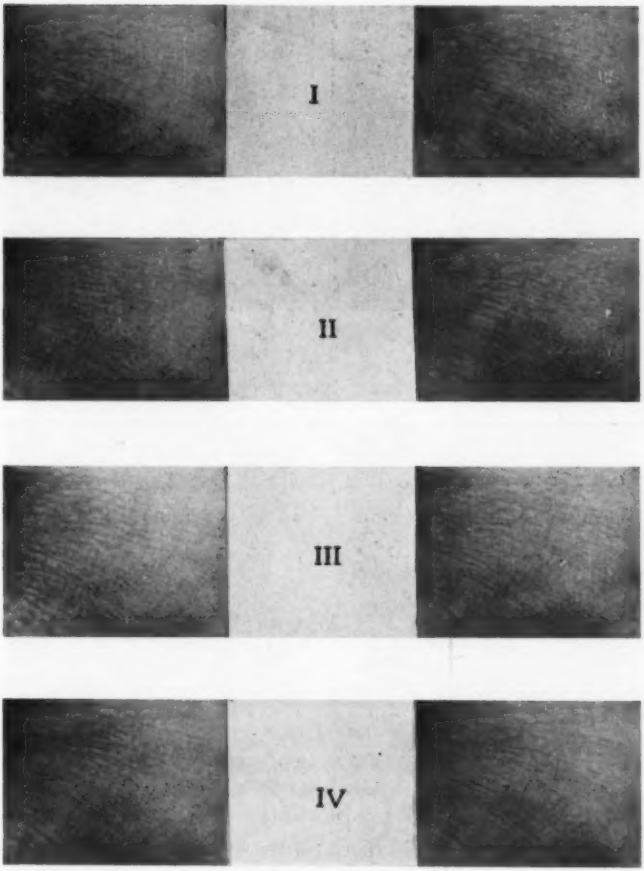


Fig. 3. Stereoscopic photographs of a calcaneus: I, base 6 cm; II, base 11 cm; III, tube moved vertically; IV, base 2 cm.

one case an image was forthcoming and in another case none appeared. All photographs were taken with the same tube, at the same distance and on the same films. In every case the voltage was 45 kV and the size of the focus 1.4 × 1.5 mm. Each was taken at a distance of 70 cm. As the phantoms were never more than ten cm thick (mostly considerably less), the variations in distinctness between elements nearer or further from the film were so minute that this factor alone could not be responsible for differences in visibility of the image. All photographs were made

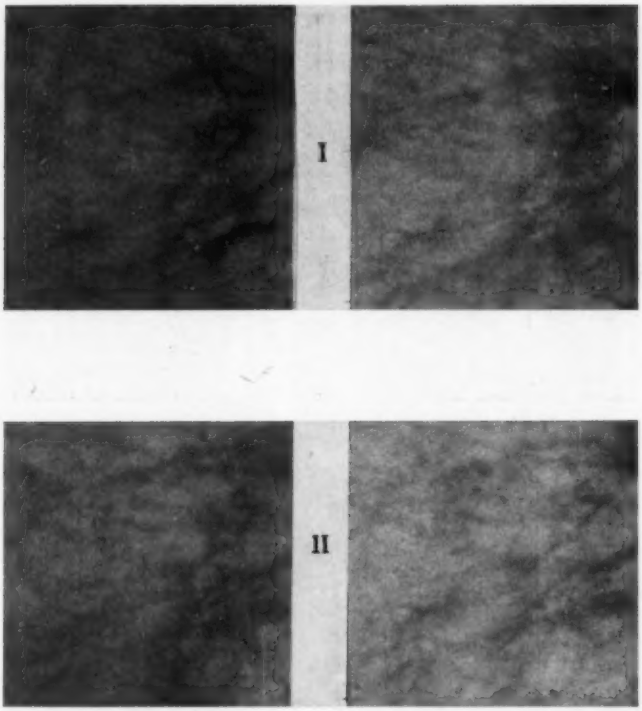


Fig. 4. Stereoscopic photographs of normal pulmonary net-work: I, base 2 cm.; II, tube moved vertically.

on Agfa-sino films and developed under exactly similar circumstances, while pictures that were to be compared with one antoher were, if possible, developed at the same time. As for observing slight contrasts the strength of the light is very important, all pictures were examined in illuminators in which the light could be regulated. Experiments were made with three kinds of phantoms.

In the tests here described all possibilities were investigated:

1. The elements of the object were entirely or almost similar or they differed in size, shape or thickness.

2. The elements were regularly or irregularly arranged.

3. The elements were just infraliminary, just supraliminary or strongly supraliminary.

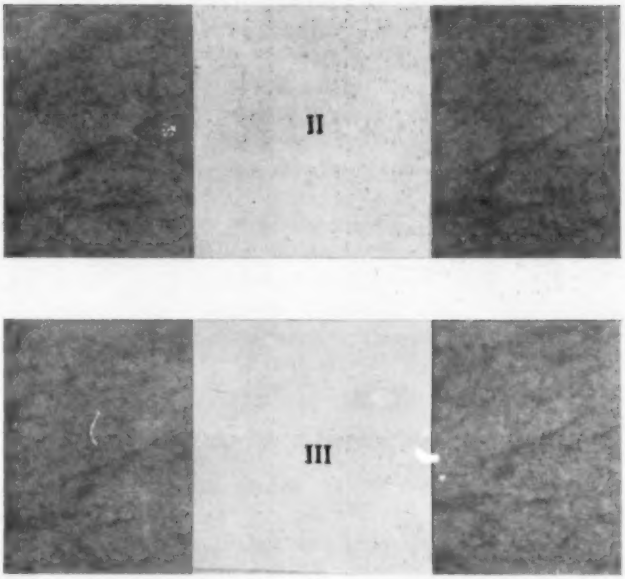


Fig. 5. Stereoscopic photographs of a lung with miliary tuberculosis: II, base 7 cm; III, tube moved vertically.

As test objects we used the following:

a. Twelve small pieces of cardboard in each of which thirty holes of equal size and similarly arranged were punched.

b. Fourteen small pieces of cardboard in each of which about thirty equal holes were punched — this time at random.

c. Twenty small pieces of cardboard on which peas were glued without any attempt at regular arrangement.

d. Irregularly shaped bits of triplex, one set of which were 5 mm and the other 2.3 mm in thickness.

Of all these series of objects photographs were made after the manner described above. In each case exposures were made of 1, 2, 3 and so forth and then of all the objects placed on top of each other. From the study of the many roentgenograms thus obtained the following rules were deduced:

I) The nature of a roentgenogram of an accumulation of many little objects depends on the contrast shown when these objects were photographed singly and under the same conditions (voltage, focus, distance and blackening of the film).

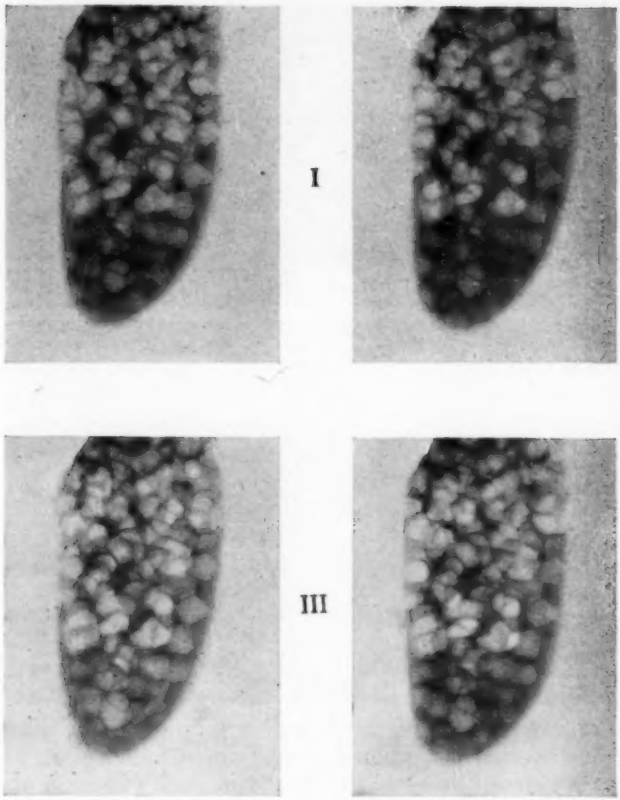


Fig. 6. Stereoscopic photographs of a gall-bladder containing 163 stones: I, base 6 cm.; III, tube moved vertically.

II) No image is obtained when a roentgenogram is made of an accumulation of many infraliminary elements of an object unless these latter are equally large and almost entirely cover each other in the direction of the rays. Except in this particular case no image is produced by the summation of the shadows of infraliminary elements.

III) In a roentgenogram of an accumulation of objects that are just supraliminary the image obtained grows less clear as the number of layers increases, until finally no distinct image is visible at all. Only when an orderly arrangement is made does a certain structure remain visible on the roentgen picture.

IV) In the case of a roentgenogram of an accumulation of many elements that are strongly supraliminary and present images equal in respect to contrasts, the picture is dominated by superposition images; here too a large number of layers causes the image to become more and more vague. When there are a large number of elements of equal size arranged in an orderly fashion, the superposition images show a regular structure of shapes which do not, however, resemble the images of the elements taken separately, unless indeed these elements cover each other entirely or at least nearly in the direction of the rays.

V) When a roentgenogram is made of an accumulation of elements the pictures of which show different contrasts, the photograph is dominated by the elements that are most supraliminary, while the remaining details either do not show at all or give rise to a vague, unanalysable background.

B. Research with a Bone Preparation

The proximal end of an unmacerated femur (caput, collum and trochanters) taken from a woman patient who died at the age of 41 was cut ventro-dorsally in thirteen slices. The slices were on an average 2.7 mm think. Owing to the process of sawing about 1 mm of the bone was lost per cut. By the aid of these slices we investigated whether or not a picture could be obtained of infraliminary details (trabeculae). Roentgenograms were taken of each slice, the object being placed on the film for 1/24, 2/24 and 3/24 of the entire period of exposure, while for the remaining fraction of the complete period the film was exposed without an object. The trabeculae were infraliminary when the slices of bone were on the film for 1/24 of the total period of exposure, while they became just supraliminary when the object remained on the film for 2/24 of the time. Further, pictures were taken of two, three, . . . to thirteen slices placed on top of each other. Now again it became evident that when these superposed slices were left on the film 1/24 of the period of exposure nothing showed on the picture. If they were left for 2/24 of the total time, bone structure always became just visible. So once more we were able to conclude that no image results from superposition of infraliminary details (trabeculae).

From these experiments we feel we may conclude as follows:

I) When on a roentgenogram the structure of the bone is visible, the image obtained cannot have been produced by trabeculae which were by nature (thickness, calcium content, for instance) or position such that each separately could not, conditions being the same, have given rise to an image.

II) Only the trabeculae which would have appeared on the picture when photographed singly under the same conditions can contribute to any picture on which bone structure is visible.

C. Stereoscopic Experiments with Anatomical Preparations

As shown by the above experiments no picture can be produced by summation of infraliminary details. It might be possible, however, that the roentgen picture of fine structures could be obtained from summation of »shadows» of supraliminary details, where the elements of the image produced by superposition strongly resemble the elements of the object. The other possibility is that these fine structures are real images, in other words, that the details that we see on the roentgenogram are pictures of certain, actually existing details of the object.

The very best means by which to investigate whether we are dealing with real images or images produced by superposition is stereoscopy. For superposition images cannot produce three-dimensional images as they do not represent objects that really exist. They might possibly give rise to fictitious solid representations, however. For, as we know, two images of structure greatly resembling each other may give rise to a »solid representation», because certain elements of the object whose position with regard to each other is pseudo-parallactic may be made to cover one another in stereoscopy, although they are no pictures of the same elements at all. But a three-dimensional image of this sort is very different from a real stereoscopic picture. It is much less quiet, because the elements of the object have no fixed place in space and seem to shift their position every now and then. A real three-dimensional representation is quiet; each element of the object has its fixed place and the observer is absolutely convinced of its existence.

Hence it follows that, in order to prove by the aid of roentgen stereoscopy that in a given case we are dealing with a real image and not with an effect due to summation, the investigator will have to prove that the picture shown is a three-dimensional representation and a real one — not fictitious.

In the experiments here described the following method was used: Stereoscopic roentgen pictures were made of several preparations. The films were covered in such a way that only an image of the fine structure (trabeculae, for instance) appeared and other (coarser) elements did not come out in the picture (such as the contour of the bone). As this made it impossible for any but small details to appear on the photograph, only these details could give rise to the stereoscopic effect. Of each preparation three pictures were taken each with a different base, *i. e.*, a different displacement of the tube. The greater the base of the exposure,

he greater the depth of the three-dimensional representation. If it is possible to determine from the depth of the pictures which was taken and which with the lesser base, then it is out of the question that we should be dealing with fictitious ones. Furthermore, we made a picture of each preparation shifting the tube slightly perpendicularly to the plane of the film instead of parallel to it. A photograph made in this way can naturally not produce a real three-dimensional representation. It might at best produce a fictitious one. So four photographs were taken of each preparation, one of which could not possibly show a three-dimensional picture, while the other three were three-dimensional images of different depths. These pictures were all shown to five experts specially trained to examine such work, who were asked to indicate which pictures showed depth and in what order they should be arranged according to size of basis, or degree of depth. The pictures were examined both orthoscopically and pseudoscopically with PLEIKART-STUMPF's stereoscope, and some observations were also made with the naked eye. In order to develop their stereoscopic powers the investigators who interpreted the pictures had been trained for some time in the examining of stereograms, special pictures having been prepared for their use in this training. Roentgen pictures of the following objects were examined according to the method described above: bone structure, net-work of the lungs, miliary tuberculosis of the lungs and a gall-bladder containing many gall-stones.

For this purpose stereoscopic roentgenograms were made as described above of different anatomical objects:

1. Bone structure: As test objects were used the proximal end of a non-macerated femur and slices of such a preparation. We also took stereoscopic roentgenograms of the calcaneus of a patient.

2. Net-work of the lungs: In the course of a post-mortem performed on a patient the whole heart and lungs were removed after the large blood-vessels had been ligatured. When the left lung had been inflated to normal size, stereograms were made of this part of the preparation.

3. The roentgen picture of miliary tuberculosis of the lungs: For this we used preparations from two patients who died of miliary tuberculosis, namely, an eight-year-old boy and a woman of thirty-nine. Here too part of the lungs was inflated.

4. The roentgen picture of gall-stones: By means of gall-stones obtained by cholecystectomy of four patients phantoms were made. In one of these a direct picture of the stones was obtained. In the others the gall-stones were made visible in the shadow of the gall-bladder by the use of umbrathor. The bladders contained 66, 163, 604 and 2,300 stones respectively.

All the experts were able to obtain a three-dimensional image in all cases in which the stereoscopic roentgenograms had been taken properly. It always proved possible to distinguish these pictures from those where the tube had been moved perpendicularly to the film. With one exception, the examiners were able to arrange the stereograms according to size of the basis. In this way it was shown objectively that with all the above roentgen pictures a real three-dimensional image can be obtained. From this it follows that in all these cases we were dealing with real images and not with superposition images.

This does not in the least contradict FRANKE's observation that the roentgen image of a bone or other object strongly resembles a section of this object. If, for instance, we compare the roentgenogram of the femur with that of a single slice, we see almost identical images. Only in the latter case the details are sharper and seem to have been photographed with greater contrast. Also pictures of 2, 3, 4 or more slices superposed present no great differences as regards the number of trabeculae. Evidently the elements of the object become more and more infraliminary as the number of layers increases, but it would seem that there are always an equal number that remain supraliminary. This appears to be due to a fact repeatedly observed, namely, that to give rise to an image the radiation contrast must be greater when there is a »background» than when there is none. Some of the trabeculae which are still visible on the roentgen picture of one slice disappear from view when there are more slices on account of the »background» of the other layers. We can therefore corroborate CHANTRAINE's statement that the picture of bone structure is not the result of summation but that, on the contrary, only those trabeculae appear on the photograph that have been able to avoid summation.

From the above experiments it does not follow, however, that all details on stereoscopic roentgen pictures are seen three-dimensionally. Because the corresponding roentgenograms are taken from different projection centres, there will always be elements in the objects which appear in the one but not in the other and these can obviously not be seen as occupying some fixed place in space. CHANTRAINE estimated the number of these at ca. 10 % of the total. At any rate they do not form a large percentage; this could not be, in view of the excellence of the three-dimensional images obtained in spite of the smallness of the picture and the convincing nature of the verifiable observations of the experts who examined them. Nor do these tests prove that absolutely no superposition images occur in roentgen pictures of bone structure. It is possible, for instance, that two elements of the object partly cover each other and so give rise to an image of one broader than either of them and representing a non-existing element. However, stereoscopic research

ustifies the statement that in the case of these or other superposition mages we are also dealing with a very small minority; for overlapping orms cannot produce three-dimensional images.

By means of stereoscopy we were able to prove that on the roentgenogram the structure of the bone, the net-work of the lungs, the image of miliary pulmonary tuberculosis and of a gall-bladder containing numerous stones were real images. The great majority of the details (such as trabeculae, miliary foci, etc.) on the roentgenogram are images of actual details in the object. Only some of the elements of the object appear on the photograph, to wit, those which, owing to their size, composition and position, are most favourably situated for roentgenography. Hence in these cases we are not dealing with summation images; on the contrary, the photograph represents those elements in the object which were able to avoid summation.

SUMMARY

The nature of roentgenograms of fine structures, in particular the structure of the bone, the lung net-work, the picture of a miliary pulmonary tuberculosis and the picture of a gall-bladder filled with many stones, was experimentally examined. Especially by stereoscopy was proved, that the roentgenograms of these fine structures are real pictures and not summation images.

ZUSAMMENFASSUNG

Die Art von Röntgenbildern feiner Strukturen, insbesondere die Knochenstruktur, die Lungenzeichnung, das Bild der miliären Lungentuberkulose und die Abbildung einer mit vielen Steinen gefüllten Gallenblase, wurde experimentell untersucht. Besonders mittels der Stereoscopie wurde bewiesen, dass Röntgenaufnahmen feiner Strukturen keine Summationsbilder sind, sondern wahre Abbildungen.

RÉSUMÉ

La nature des roentgenogrammes des structures fines, en particulier de la structure des os, du dessin pulmonaire, de la tuberculose pulmonaire miliaire et d'une vesicule biliaire avec beaucoup de calculs, fut examiné experimentalement. Avant tout par la stéréoscopie fut demontré que les roentgenogrammes des structures fines ne sont pas d'images de sommation mais des images réelles.

REFERENCES

1. H. Chantraine, Fortschr. Rö.str. 66.
2. —, Beiträge zur Klinik der Tuberkulose 98.
3. O. von Dehn and M. Weischenk, Fortschr. Rö.str. 32.
4. H. Franke, Fortschr. Rö.str. 50.
5. —, Fortschr. Rö.str. 64.
6. —, Fortschr. Rö.str. 66.
7. K. Heckmann and L. Barth, Fortschr. Rö.str. 53.
8. A. Ott, Fortschr. Rö.str. 31.
9. J. E. J. Resink, Thesis, University of Amsterdam, 1945.

FROM THE ORTHOPEDIC CLINIC OF THE CAROLINE INSTITUTE, STOCKHOLM, SWEDEN
(CHIEF: STEN FRIBERG)

FUSION OF VERTEBRAE FOLLOWING NON-INFECTIOUS DISTURBANCE IN THE ZONE OF GROWTH[1]

by

Folke Knutsson

In Scheuermann's disease there is present a disturbance in the zone of growth of the vertebral bodies. This disturbance of the increment of growth may give rise to a wedge-shaped deformation of the vertebral body, or to a vertebral body which although retaining its rectangular shape is lower than normal. On the sagittal view of the spine this disturbance of development appears as irregularities of the surface of the vertebral body. It is most conspicuous in the surroundings of the limbus nucleus. On the termination of growth there remains merely a certain wavy irregularity of the surface of the vertebral body with greater or lesser dented depressions. The intervertebral space is always retained but often rather lower than the normal.

In rare cases there occurs a similar disturbance in the zone of growth of the vertebral body, with, however, a divergent course and a different final stage. In the initial stage the affection resembles Scheuermann's disease with changes of the surface of the vertebral body in the surroundings of the limbus nucleus. In the further development the cartilage substance of the anterior portion of the intervertebral space is entirely disappeared and there occurs an osseous fusion between the vertebral bodies. In the posterior portion the cartilage plate remains and increment of growth can proceed freely in this area. In consequence of this there occurs a fusion between the vertebral bodies and owing to the increment of growth that is able to take place in the posterior portion of the vertebral bodies the fusion undergoes a progressive curvature. Finally, there thus arises a curved fusion of several vertebral bodies in which the border between the various vertebral bodies merely appears as a striate remnant of the posterior portion of the intervertebral space. If the patient in this final stage comes to roentgen examination it lies

[1] Submitted for publication, Aug. 23, 1949.

2. 7. 1947. 8. 2. 1949.

close at hand to assume a primary malformation or a sequela to an infectious spondylitis.

The disease develops insidiously with absence of pain or fever. There is no substantiation for infection. The one thing that takes place is that the back becomes more and more kyphosed and becomes stiff in the implicated area. I have had the opportunity of examining and following one such case and have in the literature found a number of entirely analogous cases (LINDEMANN, ROSENTHAL, HEIDSIECK, LEROY, SIMONS). Commonly, the fusion occurs in the lower portion of the thoracic spine.

The present case is that of a boy born 1935 (record no 3854/47). During the last 7 to 8 years a considerable kyphosis has developed within the lower portion of the thoracic spine. For the rest there is no pain or discomfort.

At examination July 2, 1947, the vertebral bodies Th. XI and Th. XII show an osseous fusion of the anterior portion; a definite disturbance of the surface of the vertebral bodies is present in the anterior portion of the intervertebral space Th. X—Th. XI. At the following examination, February 8, 1949, there has taken place an osseous fusion also between Th. X and Th. XI, and a distinct disturbance now appears in the surfaces of the vertebral bodies in the anterior portion of the intervertebral space Th. IX—Th. X, indicating that a synostosis will occur here also. Within the area of fusion there remain only lesser portions of the posterior area of the intervertebral space. The fusion has in the interval between examinations undergone curvature.

SUMMARY

A case of non-infectious disturbance in the zone of growth during the period of growth, leading to osseous fusion. The affection is of interest, inter alia from the point of view of differential diagnostics, as distinct from primary malformation or the final stage of infectious spondylitis.

ZUSAMMENFASSUNG

Ein Fall von nicht-infektiöser Störung der Wachstumszone während des Wachstums, die zu knochiger Verbindung führte. Das Leiden ist u. a. in differentialdiagnostischer Hinsicht interessant, da es von primärer Missgestaltung und von den Endstadien einer infektiösen Spondylitis unterscheidet werden soll.

RÉSUMÉ

Description d'un cas où existait un trouble, non causé par une infection, de la zone de croissance à l'âge du développement, trouble qui entraîna une fusion osseuse. L'affection est intéressante, entre autres au point de vue du diagnostic différentiel, car il faut la distinguer d'une malformation congénitale ou du stade final d'une spondylite infectieuse.

LITERATURE

LINDEMANN: Über eine eigenartige Form der Wirbelsynostose bei Kyphose im Wachstumsalter (Rö.prax. 3, 1931).

ROSENTHAL: Angeborene Kyphose (Z. orth. Chir. 53).

LINDEMANN: Bandscheibenverknöcherung bei juvenilen Kyphosen (Verh. d. deutsch. orth. Ges. 30, 1935).

LEROY: Cyphose chez un adolescent avec ossification des disques intervertébraux (Revue d'orth. 21, 1934).

HEIDSIECK: Jugendkyphose mit Wirbelverschmelzung (Verh. d. Deutsch. orth. Ges. 33, 1938).

SIMONS: Röntgendiagnostik der Wirbelsäule (Jena 1939).

FROM THE DEPARTMENT OF RADIOTHERAPY, ROYAL INFIRMARY, EDINBURGH, SCOTLAND.

WIDE FIELD IRRADIATION AND THE PLATELET COUNT[1]

by

W. M. Court Brown

Introduction

It is a recognised fact that the irradiation of large areas of the body may produce, in the absence of any skin reaction, a severe constitutional disturbance of which marrow hypoplasia is the most important feature. This is in direct contrast to the findings under the conditions of localised irradiation in which the likelihood of producing severe anaemia is much less, and in which treatment can be effectively controlled by observation of the local skin reaction. It is of paramount importance, therefore, during wide field irradiation to avoid the production of any significant degree of hypoplasia, and for this purpose it has been customary to observe during treatment either the total white cell count or the lymphocyte count.

Since 1942—43, wide field irradiation has been used to an increasingly greater extent in the Royal Infirmary, Edinburgh. At first its use was restricted to the treatment of the various types of reticuloses, but more recently it has been used on a curative basis in the treatment of certain extremely radiosensitive tumours, which tend to spread rapidly and widely at an early stage in their development. Such tumours are exemplified by seminoma of the testis, undifferentiated carcinoma of the thyroid gland (GRAHAM and MCWHIRTER) and certain forms of reticulum cell sarcoma. The most recent development is the application of wide field irradiation to the treatment of certain types of undifferentiated bronchial carcinoma.

Initially the method of control adopted was observation of the total white cell count, and it was found in the great majority of cases that this form of control was perfectly satisfactory. There was, however, a minority of cases which developed severe and sometimes fatal degrees

[1] Submitted for publication, June 30, 1949.

of anaemia after the completion of treatment apparently correctly controlled by the total white cell count. It was found impossible to predict at the beginning of treatment into which category a case would fall.

Case No. 24,983 (*Fig. 1*): A case of generalised aleukaemic reticulosis, glandular enlargement first being noted in November 1944. The patient was referred to the Radiotherapy Department for the first time in February 1946. On examination there was generalised enlargement of the superficial lymph glands, but no enlargement of liver or spleen. Histological examination of an excised gland showed that the normal lymph gland architecture had been replaced by two main cell types which occurred in more or less uniform sheets. One cell type was a mature lymphocyte, the other had characters of an undifferentiated reticulo-endothelial element. Treatment was given from 4. 3. 46 to 4. 4. 46 in the form of divided trunk baths using opposed large fields. The patient developed a severe radiation anaemia from which he recovered only after numerous blood transfusions. He subsequently died on 1. 11. 48 with gross recurrence of the disease.

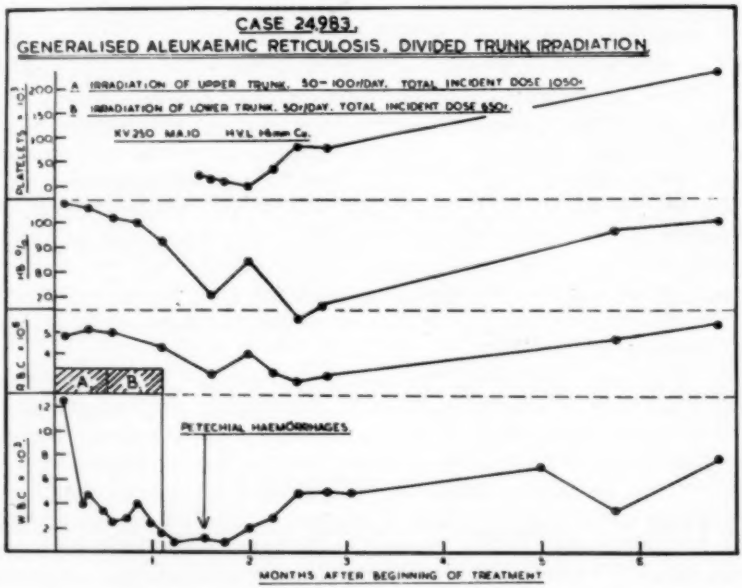

CASE 24983.
GENERALISED ALEUKAEMIC RETICULOSIS. DIVIDED TRUNK IRRADIATION
A IRRADIATION OF UPPER TRUNK. 50–100r/DAY. TOTAL INCIDENT DOSE 1050r.
B IRRADIATION OF LOWER TRUNK. 50r/DAY. TOTAL INCIDENT DOSE 850r.
KV 250 MA 10 HVL 1·8mm Cu
PLATELETS × 10³
HB %
R.B.C. × 10⁶
W.B.C. × 10³
A
B
PETECHIAL HAEMORRHAGES
MONTHS AFTER BEGINNING OF TREATMENT

Fig. 1.

A study of this case reveals three important findings. Firstly, in spite of adequate control by the total white cell count a severe anaemia did ultimately develop. Secondly, petechial haemorrhages occurred shortly after the end of treatment preceding the full development of the anaemia, and thirdly, the anaemia was associated with a very low platelet count.

With the development of the curative treatment by wide field irradiation of certain very radiosensitive forms of tumour, and as the level of dosage administered in these cases was dangerously high, it became essential to establish a more reliable method of control than had hitherto been used, and which was applicable to all cases. The great similarity between the haemorrhagic features of the syndrome of radiation anaemia and those of acute idiopathic thrombocytopenic purpura suggested that it might be profitable to investigate the effect of wide field irradiation on the platelet count. It was decided to carry out routine platelet counts on every patient submitted to wide field irradiation to determine in the first place the effect on the count, and in the second place the possible value of the count as an indicator in comparison with the proven values of the total white cell and differential counts. During the investigation considerable encouragement was obtained from the work of MOSSBERG on the behaviour of the platelet count in response to localised irradiation.

On the advice of Professor L. S. P. DAVIDSON a direct method of platelet enumeration was adopted, which in the hands of skilled technicians has yielded remarkably consistent results. Using this technique the average range of normal has been found to be from 200,000 to 400,000 platelets per cubic millimetre, and the experimental error of the order of $\pm$ 25,000 platelets per cubic millimetre (for full details see appendix).

In the early stages of the investigation the cases treated were those of the reticulosis group many of which showed evidence of abnormal and impaired haemopoiesis, but recently the treatment of the radiosensitive carcinomata has provided an opportunity of studying the platelet response in the presence of normal haemopoiesis. In addition at the beginning of the investigation attention was mainly focussed on the findings towards the end of treatment, but latterly it has been found that important and significant changes in the count occur shortly after the commencement of treatment. It is now possible, therefore, to present a fairly complete picture of the response of the platelet count to wide field irradiation under a wide variety of conditions.

The Effect of Wide Field Irradiation no the Platelet Count

Cases with Normal Haemopoiesis

The majority of cases — approximately 70 % — show a consistent and distinctive type of response in which two separate peak values occur shortly after the beginning of treatment, and are then followed by a steady fall in the count (Fig. 2). The first peak value has been found to occur usually before the sixth day after the beginning of treatment, being most frequently noted before the third day, while the second peak

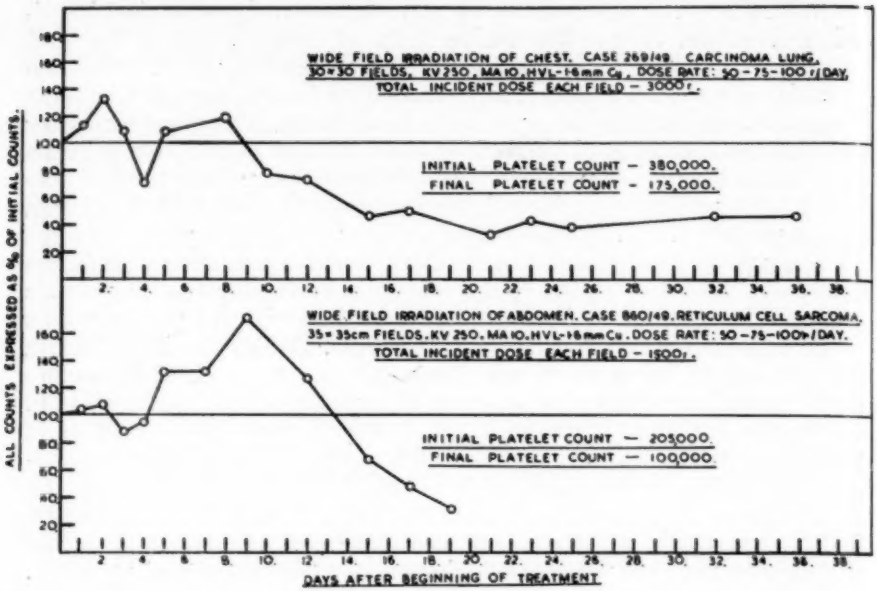

WIDE FIELD IRRADIATION OF CHEST. CASE 269/49. CARCINOMA LUNG.
30×30 FIELDS. KV 250. MA 10. HVL-1·6 mm Cu. DOSE RATE: 50-75-100 r/DAY.
TOTAL INCIDENT DOSE EACH FIELD - 3000 r.
INITIAL PLATELET COUNT - 380,000.
FINAL PLATELET COUNT - 175,000.
WIDE FIELD IRRADIATION OF ABDOMEN. CASE 860/49. RETICULUM CELL SARCOMA.
35×35cm FIELDS. KV 250. MA 10. HVL-1·6 mm Cu. DOSE RATE: 50-75-100 r/DAY.
TOTAL INCIDENT DOSE EACH FIELD - 1500 r.
INITIAL PLATELET COUNT — 205,000.
FINAL PLATELET COUNT — 100,000.
ALL COUNTS EXPRESSED AS % OF INITIAL COUNTS.
DAYS AFTER BEGINNING OF TREATMENT

Fig. 2.

value has been found to occur between the fourth and sixteenth days inclusively, and to be most frequent between the fifth and tenth days inclusively (Fig. 3). The magnitudes of both peaks vary considerably, from 105 % to 200 % of the pre-irradiation count, but in a proportion of cases either peak value may not be as great as the pre-irradiation value

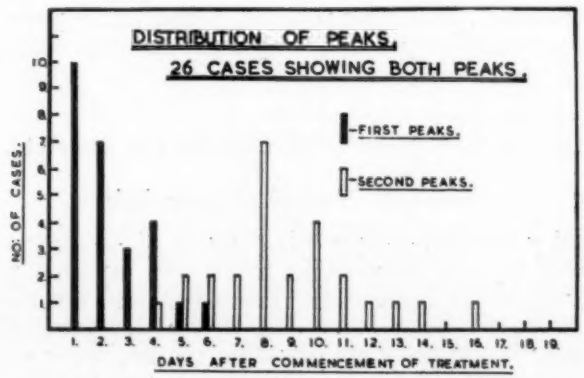


Fig. 3.

of the count. This has been found to occur in about 12 % of the first peaks, and in about 30 % of the second peaks, and for the purposes of description such peaks can be called »negative» peaks. It has not been possible so far to show any correlation between the magnitude of any one peak and the radiation tolerance of the individual concerned. It is safe, however, to make the general statement that if both peaks are high the tolerance of the individual is likely to be within the limits of normal for the irradiation technique used, but if both are negative it is likely that tolerance will be low.

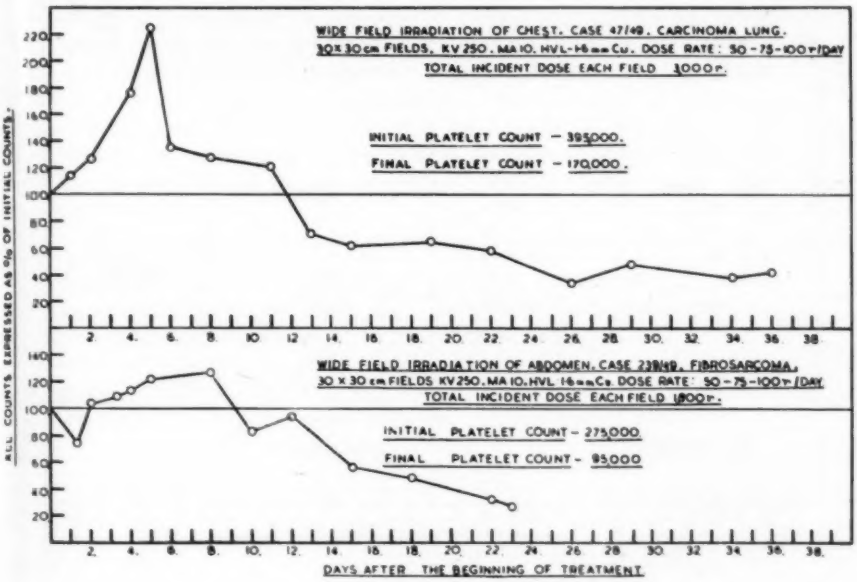

WIDE FIELD IRRADIATION OF CHEST. CASE 47/49. CARCINOMA LUNG.
30x30 cm FIELDS, KV 250. MA 10. HVL-1·6 mm Cu. DOSE RATE: 50-75-100 r/DAY
TOTAL INCIDENT DOSE EACH FIELD 3000 r.
INITIAL PLATELET COUNT - 385000.
FINAL PLATELET COUNT - 170000.
WIDE FIELD IRRADIATION OF ABDOMEN. CASE 238/49. FIBROSARCOMA.
30 x 30 cm FIELDS KV 250. MA 10. HVL 1·6 mm Cu. DOSE RATE: 50-75-100 r/DAY
TOTAL INCIDENT DOSE EACH FIELD 1800 r.
INITIAL PLATELET COUNT - 275000
FINAL PLATELET COUNT - 95000
ALL COUNTS EXPRESSED AS % OF INITIAL COUNT
DAYS AFTER THE BEGINNING OF TREATMENT

Fig. 4.

In a minority of cases — approximately 30 % — the response is modified, and only a single peak is found (Fig. 4). It would appear justifiable to assume that in some cases this may be due to the superimposition of the more common two peaks producing a summated effect, and in others to a failure to demonstrate with counts at twenty-four hourly intervals the presence of the first peak. The magnitudes of the peak values in this type of response have been found to vary from 127 % to 252 % of the pre-irradiation platelet level. No significant difference has been found in the ultimate behaviour of these cases.

After the characteristic peaks have occurred the platelet count shows a steady fall which has been found to be exponential in character (Fig. 5). The steepness of this fall is expressed in terms of the gradient of the line which best fits the points obtained by plotting the natural logarithm of the percentage platelet value against the time in days ($\tan \theta$). As might be expected the values of $\tan \theta$ for the larger areas irradiated tend to be greater than those of the smaller areas irradiated. Thus comparing the fall of the count in the extremes of field size in common use, and taking those cases found to have a normal radiation tolerance and

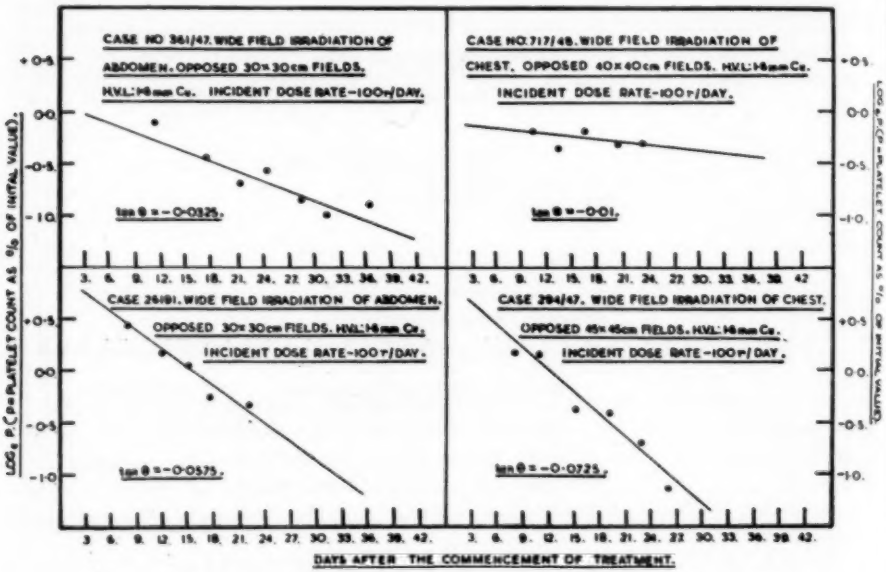

CASE NO 361/47. WIDE FIELD IRRADIATION OF ABDOMEN. OPPOSED 30×30cm FIELDS. HVL: 1·6 mm Cu. INCIDENT DOSE RATE-100 r/DAY.
tan θ = -0·0325.
CASE NO 717/46. WIDE FIELD IRRADIATION OF CHEST. OPPOSED 40×40cm FIELDS. HVL: 1·6 mm Cu. INCIDENT DOSE RATE-100 r/DAY.
tan θ = -0·01.
CASE 26/81. WIDE FIELD IRRADIATION OF ABDOMEN. OPPOSED 30×30cm FIELDS. HVL: 1·6 mm Cu. INCIDENT DOSE RATE-100 r/DAY.
tan θ = -0·0575.
CASE 284/47. WIDE FIELD IRRADIATION OF CHEST. OPPOSED 45×45cm FIELDS. HVL: 1·6 mm Cu. INCIDENT DOSE RATE-100 r/DAY.
tan θ = -0·0725.
DAYS AFTER THE COMMENCEMENT OF TREATMENT.

Fig. 5.

which were irradiated with a daily incident dose of 100 r on each of two opposed fields using a beam of Half Value Layer of 1.6 mm. Cu, the following ranges of value of $\tan \theta$ have been found:

30 × 30 cm. Fields.

Range of value of $\tan \theta$ = —0.004 — —0.045
Mean value of $\tan \theta$ = —0.0238

45 × 45 cm. Fields.

Range of value of $\tan \theta$ = —0.0625 — —0.095
Mean value of $\tan \theta$ = —0.0755

The difference between the means is statistically significant.

(A case is said to have normal radiation tolerance if in the case of 30 × 30 cm. fields a maximum incident dose in both fields of 2,200 r is given before the platelet level falls to 100,000 platelets per cubic millimetre. For 45 × 45 cm. fields the value is 1,500 r. These figures, which may be called »average tolerance doses», are obtained from spot graphs — see Fig. 7.)

Establishment of the Safety Level.

At an early stage in the investigation it became desirable to establish a minimum level, henceforward known as the safety level, below which reduction of the platelet count would carry the risk of the development of a significant degree of anaemia. To do this it was necessary to carry out both platelet and total white cell counts on a series of cases, but only to observe the white cell count as the method of control. In the light of the peripheral blood counts both during treatment and in the immediate post-treatment period it became possible to assess the level of the platelet count which would be most likely to ensure the safety of the patient. A typical case is shown in Fig. 6. It will be seen that the patient commenced the second part of his treatment in a state of

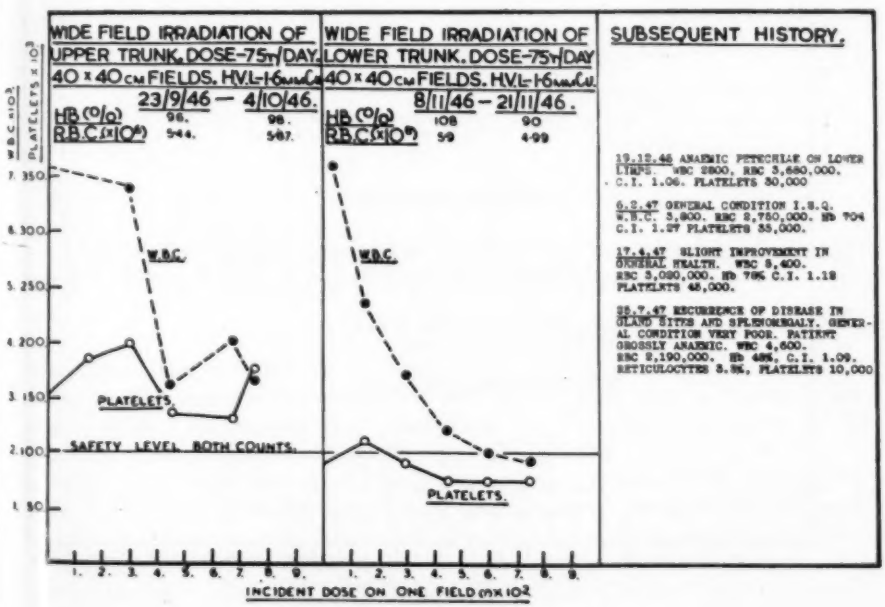

WIDE FIELD IRRADIATION OF UPPER TRUNK. DOSE-75r/DAY. 40 x 40 cm FIELDS. HVL-16mm Cu
23/9/46 — 4/10/46.
HB (%) 98. 98.
R.B.C. (10⁶) 5·44. 5·87.
WIDE FIELD IRRADIATION OF LOWER TRUNK. DOSE-75r/DAY 40 x 40 cm FIELDS. HVL-16mm Cu.
8/11/46 — 21/11/46.
HB (%) 108 90
R.B.C. (10⁶) 5·9 4·09
SUBSEQUENT HISTORY.
19.12.46 ANAEMIC PETECHIAE ON LOWER LIMBS. WBC 2800, RBC 3,680,000. C.I. 1.06. PLATELETS 80,000
6.2.47 GENERAL CONDITION I.S.Q. W.B.C. 3,800. RBC 2,750,000. Hb 70% C.I. 1.27 PLATELETS 55,000.
17.4.47 SLIGHT IMPROVEMENT IN GENERAL HEALTH. WBC 9,400. RBC 3,000,000. Hb 78% C.I. 1.18 PLATELETS 48,000.
28.7.47 RECURRENCE OF DISEASE IN GLAND SITES AND SPLENOMEGALY. GENERAL CONDITION VERY POOR. PATIENT GROSSLY ANAEMIC. WBC 4,600. RBC 2,190,000. Hb 48%. C.I. 1.09. RETICULOCYTES 8.9%, PLATELETS 10,000
W.B.C. x10³
PLATELETS x 10³
7. 350
6. 300
5. 250
4. 200
3. 150
2. 100
1. 50
W.B.C.
PLATELETS
SAFETY LEVEL BOTH COUNTS.
1. 2. 3. 4. 5. 6. 7. 8. 9.
INCIDENT DOSE ON ONE FIELD (r) x 10²

Fig. 6.

thrombocytopenia though the level of the total white cell count suggested that further irradiation could be safely given. The platelet level during treatment was almost constantly depressed below the value of 100,000 platelets per cubic millimetre, and the patient subsequently developed the classical picture of radiation anaemia. As a result of such experiences and on the advice of Professor L. S. P. DAVIDSON it was decided to adopt the value of 100,000 platelets per cubic millimetre as the safety level. It is not known what is the actual critical level for the development of anaemia, but it does appear to be below this value, and it will probably vary between individuals and for different types of disease. Since the establishment of this level there has not been any occasion to revise it.

The Effect of Variation of the Area Irradiated and of the Incident Dose Rate on the Fall of the Platelet Count to the Safety Level.

It has already been demonstrated that when large field sizes are irradiated the rate of fall of the platelet count is greater than during the irradiation of the smaller field sizes. This is further emphasized in Fig. 7 which shows that during the irradiation of the larger field sizes treatment was stopped in a significantly greater number of cases because of

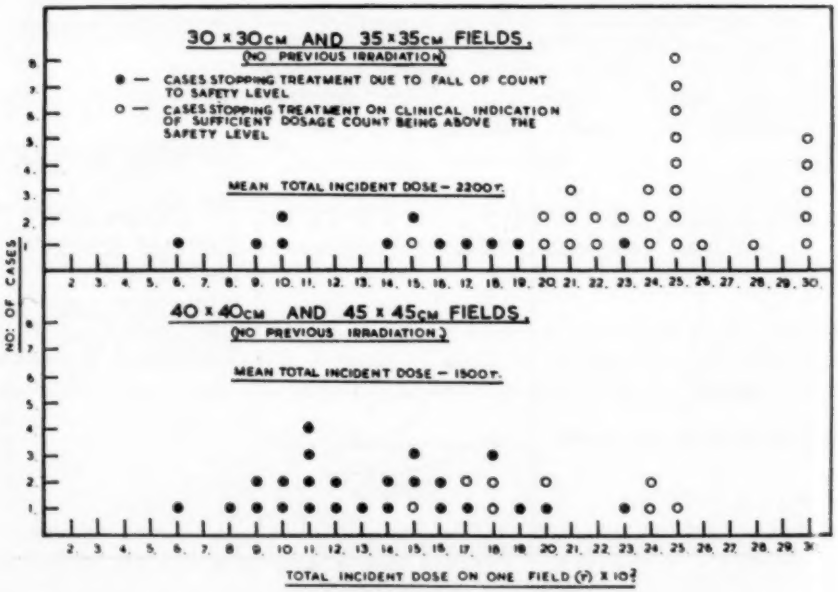

30 x 30CM AND 35 x 35CM FIELDS.
(NO PREVIOUS IRRADIATION)
● — CASES STOPPING TREATMENT DUE TO FALL OF COUNT TO SAFETY LEVEL
○ — CASES STOPPING TREATMENT ON CLINICAL INDICATION OF SUFFICIENT DOSAGE COUNT BEING ABOVE THE SAFETY LEVEL
MEAN TOTAL INCIDENT DOSE – 2200r.
NO: OF CASES
40 x 40CM AND 45 x 45CM FIELDS.
(NO PREVIOUS IRRADIATION)
MEAN TOTAL INCIDENT DOSE – 1500r.
TOTAL INCIDENT DOSE ON ONE FIELD (r) X 10²

Fig. 7.

a fall in the count to the safety level, than was the case when the smaller field sizes were treated. It has not been customary during treatment to increase the field size, but it is safe to presume that were this done the rate of fall of the count would be increased, thus increasing the value of tan θ.

Reduction of the area irradiated and reduction of the incident dose rate produce the same effect on the count, shown by a significantly reduced rate of fall, and it is presumed that there is a corresponding increase in the radiation tolerance of the individual (Fig. 8). It is found

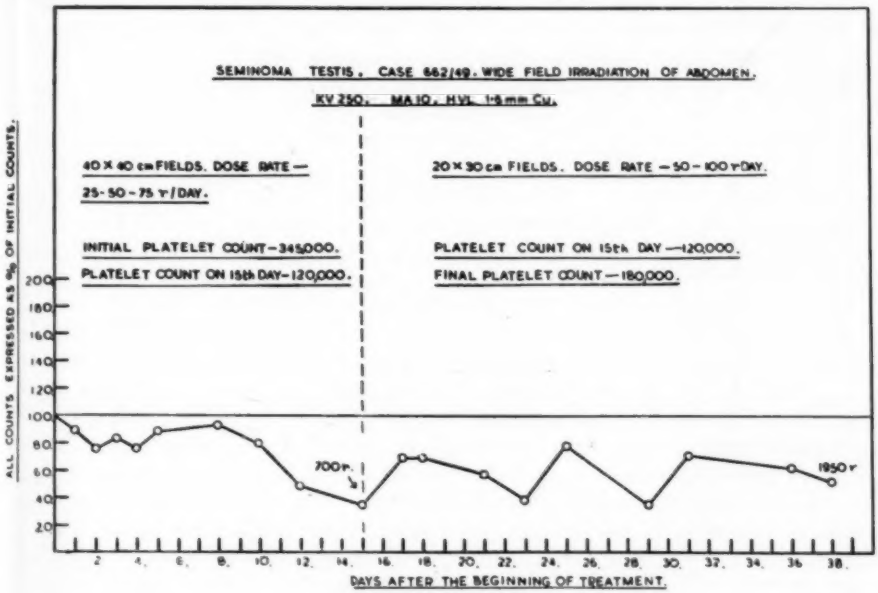

SEMINOMA TESTIS. CASE 662/49. WIDE FIELD IRRADIATION OF ABDOMEN.
KV 250. MA 10. H.V.L. 1·5 mm Cu.
40 × 40 cm FIELDS. DOSE RATE — 25-50-75 r/DAY.
INITIAL PLATELET COUNT — 345,000.
PLATELET COUNT ON 15th DAY — 120,000.
20 × 30 cm FIELDS. DOSE RATE — 50-100 r/DAY.
PLATELET COUNT ON 15th DAY — 120,000.
FINAL PLATELET COUNT — 180,000.
700 r.
1950 r.
ALL COUNTS EXPRESSED AS % OF INITIAL COUNTS.
DAYS AFTER THE BEGINNING OF TREATMENT.

Fig. 8.

that when this occurs the platelet count tends to show widely fluctuating values due to the formation of small clumps and a tendency for the platelets to be unevenly distributed in the counting chamber. It should be noted that the platelet count will only respond in this way to a reduction in dose rate or of irradiated volume provided that the original dose rate and volume irradiated have not seriously reduced the patient's radiation tolerance. When this has occurred then even on the cessation of treatment there will be a lag period during which the count continues to fall before recovery takes place, and during this lag period radiation anaemia may supervene.

Cases with Impaired Haemopoiesis.

The alteration in response in these cases is quantitative rather than qualitative, the most significant change being in the ultimate rate of fall of the count. Thus in a group of cases with impaired tolerance, excluding leukaemias and comprising mainly cases having had previous extensive irradiation, the values of tan θ showed a range of -0.055 to -0.27 with a mean value of -0.1203. This mean value is significantly higher than either of those already quoted for the extremes of field size in cases with normal tolerance. As a secondary consideration there may

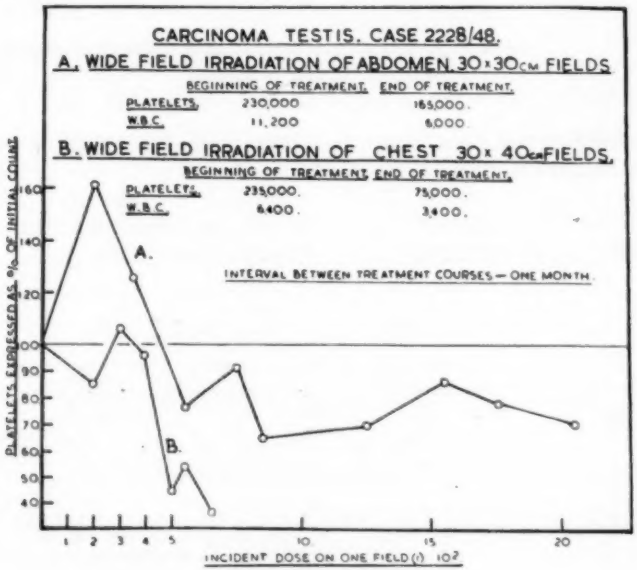


Fig. 9.

be quantitative changes in the characteristic peak values, and it is more common to find negative second peaks in this group than in the groups with normal tolerance.

There is no doubt that previous extensive irradiation does severely impair an individual's radiation tolerance and this is well demonstrated by the platelet count (Fig. 9).

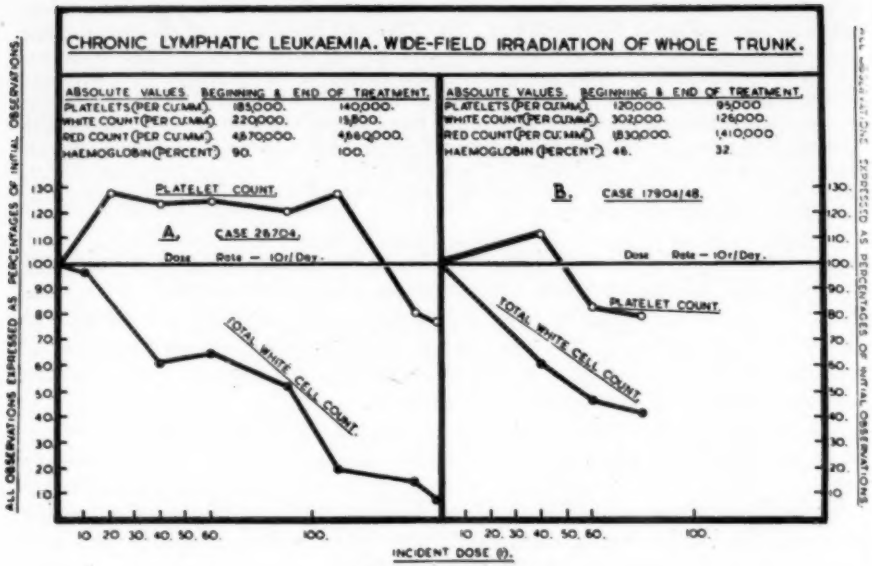
Case No. 2228/48 (*Fig. 9*): Patient referred to Radiotherapy Department on 7. 10. 48, a swelling of the left testicle having been noted since 1934. Pre-operative examination showed a swelling of the left testis measuring 7 × 9 cm., but no obvious involvement of the cord. An ill-defined glandular mass was palpable in the upper abdomen,

and several small glands 0.5 cm. in diameter were present in the left posterior cervical chain. Aschheim-Zondek Test weakly positive. Roentgen examination of the chest showed an ill-defined shadow in the right lower lung field, the appearances suggesting metastases. 4. 10. 48 — Left orchidectomy and excision of a gland from left posterior cervical chain. Histological examination showed a teratoma of the testis complicated by an embryonal carcinoma and secondary involvement of the gland. In view of the dissemination of the disease, it was decided to treat the abdomen by wide field irradiation following after an interval with wide field irradiation of the chest and neck. As will be seen from Fig. 9, the second half of treatment was terminated after only a low dose had been given owing to a fall in the platelet count.

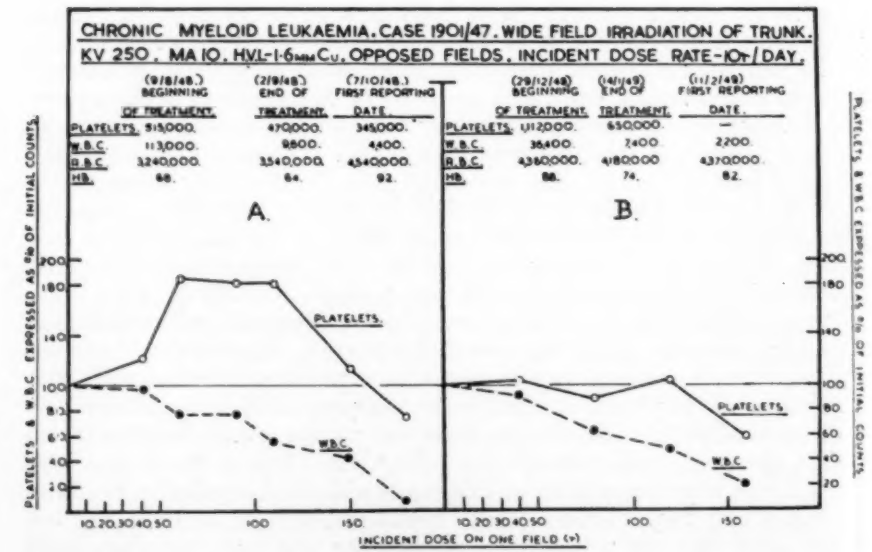
It is a very significant fact that these cases may show no evidence of impaired tolerance when examination of the blood picture is confined to observation of the total white cell and lymphocyte counts, and the first indication of the presence of this pre-existing damage under this latter form of control is likely to be the development of a severe anaemia after the cessation of treatment.

The type of case with neoplastic involvement of bone marrow which may be associated with impaired tolerance is best shown by a consideration of chronic lymphatic and chronic myeloid leukaemia. In chronic lymphatic leukaemia, in the absence of any significant degree of anaemia prior to the beginning of treatment, the characteristic response is a rise in the platelet count which may be prolonged for a considerable period before a fall towards the safety level occurs (Fig. 10 A). In the presence of severe anaemia however wide field irradiation produces a limited peak and subsequently a rapid fall to the platelet level (Fig. 10 B).

It has been found in chronic myeloid leukaemia that the average platelet count before treatment tends to be high, and that throughout the development of the disease in any one case the average count tends to rise, sometimes reaching very high levels. It is only in the terminal phase of marrow failure that the count falls. In the early stages of the development of the disease wide field irradiation produces a considerable increase in the level of the count which is maintained for a long period of time, but is finally replaced by a fall towards the safety level if irradiation is continued for a sufficient period of time (Fig. 11 A). When this type of response is obtained one can confidently expect a considerable improvement in the values of the haemoglobin level and the red cell count, and a satisfactory and sometimes prolonged remission. During the intermediate phases of the disease the platelet level is usually very high and wide field irradiation does not produce any significant rise before the count falls towards the safety level (Fig. 11 B). It has been our general experience that at this stage wide field irradiation produces no significant improvement in the haemoglobin level and the red cell count, and that the periods of remission are much shorter than in the earlier phase. In the terminal phase wide field irradiation causes a rapid


CHRONIC LYMPHATIC LEUKAEMIA. WIDE-FIELD IRRADIATION OF WHOLE TRUNK.
ABSOLUTE VALUES. BEGINNING & END OF TREATMENT.
PLATELETS (PER CU MM). 185,000. 140,000.
WHITE COUNT (PER CU MM). 220,000. 15,800.
RED COUNT (PER CU MM). 4,870,000. 4,860,000.
HAEMOGLOBIN (PERCENT). 90. 100.
ABSOLUTE VALUES. BEGINNING & END OF TREATMENT.
PLATELETS (PER CU MM). 120,000. 95,000
WHITE COUNT (PER CU MM). 302,000. 126,000.
RED COUNT (PER CU MM). 4,830,000. 4,410,000
HAEMOGLOBIN (PERCENT). 48. 32.
A, CASE 26704.
Dose Rate — 10r/Day.
PLATELET COUNT.
TOTAL WHITE CELL COUNT.
B, CASE 17904/48.
Dose Rate — 10r/Day.
PLATELET COUNT.
TOTAL WHITE CELL COUNT.
ALL OBSERVATIONS EXPRESSED AS PERCENTAGES OF INITIAL OBSERVATIONS.
INCIDENT DOSE (r).

Figs. 10 A and B.


CHRONIC MYELOID LEUKAEMIA. CASE 1901/47. WIDE FIELD IRRADIATION OF TRUNK.
KV 250. MA 10. HVL-1·6mm Cu. OPPOSED FIELDS. INCIDENT DOSE RATE-10r/DAY.
(9/8/48.) BEGINNING OF TREATMENT.
(2/9/48.) END OF TREATMENT.
(7/10/48.) FIRST REPORTING DATE.
PLATELETS. 515,000. 470,000. 345,000.
W.B.C. 113,000. 9800. 4400.
R.B.C. 3240,000. 3540,000. 4540,000.
Hb. 68. 84. 92.
(29/12/48) BEGINNING OF TREATMENT.
(14/1/49) END OF TREATMENT.
(11/2/49) FIRST REPORTING DATE.
PLATELETS. 1112,000. 650,000. —
W.B.C. 36400. 2400. 2200.
R.B.C. 4360,000. 4180,000. 4370,000.
Hb. 88. 74. 82.
A.
B.
PLATELETS.
W.B.C.
PLATELETS & W.B.C. EXPRESSED AS % OF INITIAL COUNTS.
INCIDENT DOSE ON ONE FIELD (r)

Figs. 11 A and B.

fall in the platelet level, and in spite of a satisfactory response on the part of the white cell count a steady deterioration in the haemoglobin level and red cell count occurs (Fig. 12).

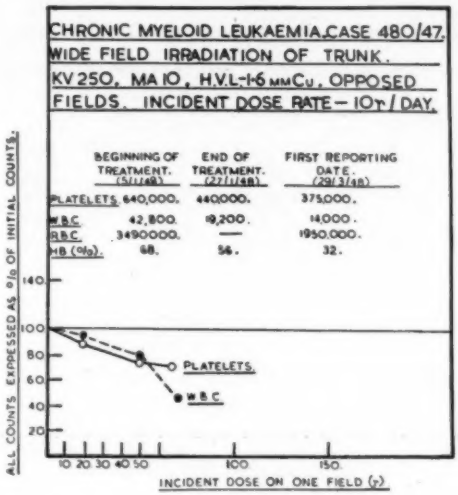

CHRONIC MYELOID LEUKAEMIA CASE 480/47.
WIDE FIELD IRRADIATION OF TRUNK.
KV 250, MA 10, H.V.L. 1·6 mm Cu, OPPOSED FIELDS. INCIDENT DOSE RATE – 10r / DAY.
BEGINNING OF TREATMENT. (5/1/48)
END OF TREATMENT. (27/1/48)
FIRST REPORTING DATE. (29/3/48)
PLATELETS 640,000. 440,000. 375,000.
W.B.C. 42,800. 19,200. 14,000.
R.B.C. 3490000. — 1950,000.
HB (%). 68. 56. 32.
ALL COUNTS EXPRESSED AS % OF INITIAL COUNTS.
140
100
80
60
40
20
PLATELETS.
W.B.C.
10 20 30 40 50 100 150.
INCIDENT DOSE ON ONE FIELD (r)

Fig. 12.

The Relative Values of the Platelet, Total White Cell and Lymphocyte Counts as Biological Indicators in Non-Leukaemic Cases

Comparison of the Platelet Count with the Total White Cell Count.

The level of 2,000 total white cells per cubic millimetre has been accepted as the safety level, and when the two counts are compared three general types of comparison are obtained.

In the first type both counts reach their respective safety levels at approximately the same time, and both are considered to be of equal value as indicators of the point to terminate treatment (Fig. 13). The majority of cases fall into this group and it is suggested that it is because the counts are of equal value that the total white cell count has been found to be so useful in a great number of cases.

In the second general type the total white cell count falls to the safety level before the platelet count, and while it may then sometimes show a maintained rise it frequently does not do so, remaining on the safety level for some time before falling to an even lower level (Fig. 14).

Case No. 2149/48 (*Fig. 14*): The patient was referred to the Radiotherapy Department in September, 1948, with a history of lumbo-sacral pain radiating towards the left hip joint since April 1947. On examination a hard fixed mass was present in the left iliac

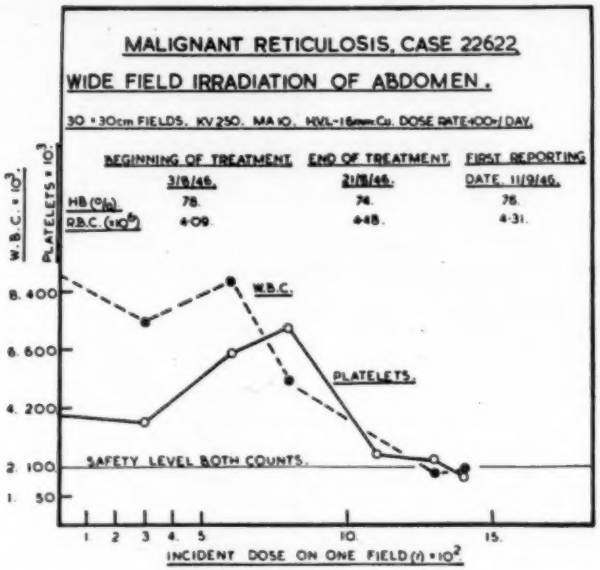

MALIGNANT RETICULOSIS, CASE 22622
WIDE FIELD IRRADIATION OF ABDOMEN.
30 × 30cm FIELDS. KV 250. MA 10. HVL-1·6mm Cu. DOSE RATE 400r/DAY.
BEGINNING OF TREATMENT
END OF TREATMENT.
FIRST REPORTING
3/9/46.
21/9/46.
DATE. 11/9/46.
HB (%)
78.
74.
78.
R.B.C. (×10⁶)
4·09.
4·48.
4·31.
W.B.C. = 10³.
PLATELETS = 10³
8. 400
6. 600
4. 200
2. 100
1. 50
W.B.C.
PLATELETS.
SAFETY LEVEL BOTH COUNTS.
1 2 3 4. 5 10. 15.
INCIDENT DOSE ON ONE FIELD (r) × 10²

Fig. 13.

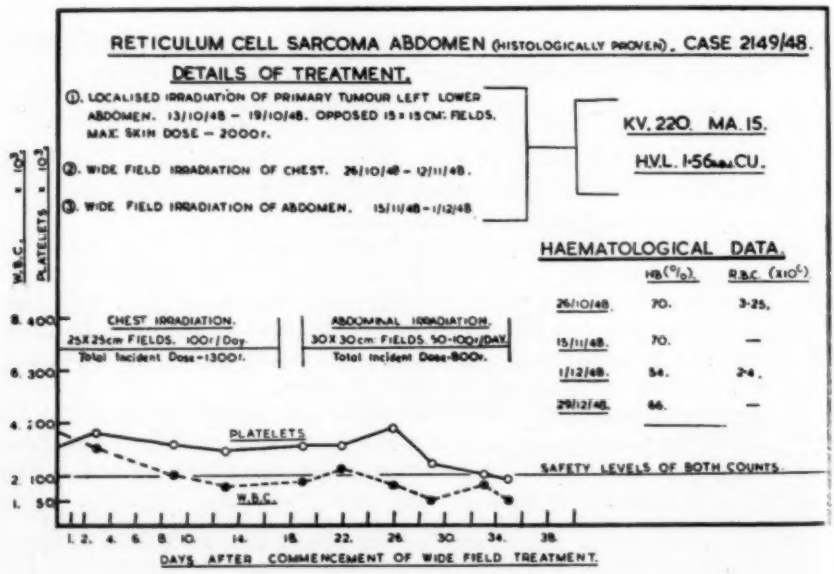

RETICULUM CELL SARCOMA ABDOMEN (HISTOLOGICALLY PROVEN). CASE 2149/48.
DETAILS OF TREATMENT.
① LOCALISED IRRADIATION OF PRIMARY TUMOUR LEFT LOWER ABDOMEN. 13/10/48 – 19/10/48. OPPOSED 15 × 15 CM. FIELDS. MAX. SKIN DOSE – 2000r.
② WIDE FIELD IRRADIATION OF CHEST. 26/10/48 – 12/11/48.
③ WIDE FIELD IRRADIATION OF ABDOMEN. 15/11/48 – 1/12/48.
KV. 220. MA. 15.
H.V.L. 1·56mm CU.
HAEMATOLOGICAL DATA.
HB (%).
R.B.C. (×10⁶)
26/10/48. 70. 3·25.
15/11/48. 70. —
1/12/48. 54. 2·4.
29/12/48. 66. —
W.B.C. = 10³.
PLATELETS = 10³
CHEST IRRADIATION. 25X25cm FIELDS. 100r/Day. Total Incident Dose = 1300r.
ABDOMINAL IRRADIATION. 30X30cm FIELDS. 50-100r/DAY. Total Incident Dose 800r.
8. 400
6. 300
4. 200
2. 100
1. 50
PLATELETS
W.B.C.
SAFETY LEVELS OF BOTH COUNTS.
1. 2. 4. 6. 8. 10. 14. 18. 22. 26. 30. 34. 38.
DAYS AFTER COMMENCEMENT OF WIDE FIELD TREATMENT.

Fig. 14.

Lymphadenoma. Case 130/48. Wide field irradiation of abdomen 19. 4. 49—25. 4. 49. Opposed 30 × 30 cm. fields. K. V. 250. M. A. 10. H. V. L. 1.6 mm. Cu. Incident dose rate — 50 — 75 — 100 r/day.

Day after the beginning of treatment	Total incident dose on one field (r)	Platelets (safety level 100,000)	Total white cell count (safety level 2,000)	Lymphocyte count (safety level 300)	HB %	Red cell count
0	50	205,000	12,800	1,920	55	2,530,000
1	100	155,000	12,600	1,530	—	—
2	150	200,000	10,800	1,300	—	—
3	225	130,000	11,400	1,030	—	—
4	300	130,000	12,000	1,560	—	—
6	400	75,000	10,100	1,520	—	—
7	—	75,000	9,800	1,380	50	2,610,000

Previous irradiation (K. V. 250. M. A. 10. H. V. L. 1.6 mm Cu).

21. 1. 48—18. 2. 48 Wide field irradiation of upper trunk. Total incident dose — 1,500 r.

19. 2. 48 Single treatment to both groins — Surface dose 1,000 r.

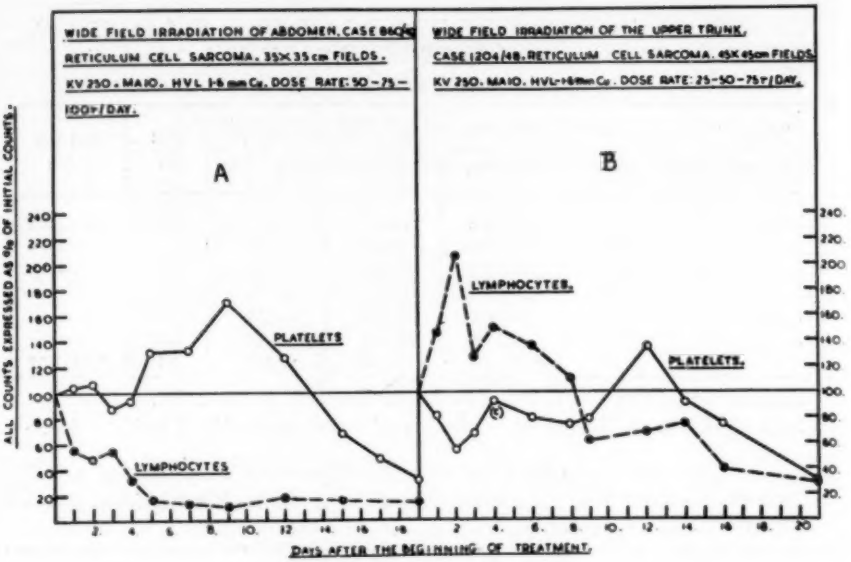
25. 3. 48—13. 4. 48 Wide field irradiation of lower trunk. Total incident dose — 750 r.

Fig. 15.

fossa measuring 11 × 7 cm. Roentgen examination showed an osteolytic defect in the left ilium, and a metastatic deposit in the left lung. Histological examination of a biopsy specimen from the pelvic mass revealed a completely undifferentiated tumour. On the presumption that the tumour might be a reticulum cell sarcoma localised irradiation was given to the pelvic mass from 13. 10. 48 to 19. 10. 48 to test its radio-sensitivity. At the completion of this treatment the tumour apparently had disappeared. Wide field irradiation of the chest was then commenced, and when radiographic evidence indicated disappearance of the lung metastasis wide field irradiation of the abdomen was undertaken. At present the patient is alive and well, and roentgen examination shows new bone formation in the region of the defect in the left ilium.

The most significant point about this case is that the tumour was most probably of the very radio-sensitive type of reticulum cell sarcoma, possibly curable by wide field irradiation even in the presence of lung metastases. If treatment had been stopped when the total white cell count had reached its safety level it is extremely doubtful whether it would have been possible to administer a dose likely to be curative. It will be noted that the patient did not develop any significant degree of anaemia.

In the third general type of comparison the platelet count falls more rapidly than the total white cell count. Into this group fall those cases which have had previous extensive irradiation (Fig. 15).


WIDE FIELD IRRADIATION OF ABDOMEN. CASE 86/48
RETICULUM CELL SARCOMA. 35×35 cm FIELDS.
KV 250. MA 10. HVL 1·6 mm Cu. DOSE RATE: 50–75–100r/DAY.
A
WIDE FIELD IRRADIATION OF THE UPPER TRUNK.
CASE 1204/48. RETICULUM CELL SARCOMA. 45×45cm FIELDS.
KV 250. MA 10. HVL 1·6 mm Cu. DOSE RATE: 25–50–75r/DAY.
B
ALL COUNTS EXPRESSED AS % OF INITIAL COUNTS.
PLATELETS
LYMPHOCYTES
LYMPHOCYTES.
PLATELETS.
DAYS AFTER THE BEGINNING OF TREATMENT.

Figs. 16 A and B.

Case No. 130/48 (*Fig. 15*): The patient was first referred to Radiotherapy department in January 1948, enlarged glands having been noted in both groins and the right axilla since August 1947. On examination there were numerous glands on both sides of the neck, in both axillae and in both groins. Histological examination of an excised gland indicated the presence of lymphadenoma. Wide field roentgen therapy was given from 21. 1. 48 to 18. 2. 48 and from 25. 3. 48 to 13. 4. 48 as indicated in the figure. The patient failed to report for follow-up examination until 14. 4. 49 when he was found to be in the terminal stages of the disease with the typical associated constitutional upset. Wide field irradiation of the abdomen was attempted to allay the skin irritation but abandoned on account of poor radiation tolerance as shown by the platelet count.

It cannot, of course, be proved that in such cases an anaemia would develop if the falling platelet count were ignored. If, however, the general premise is accepted that the platelet count is a more sensitive indicator of haemopoietic tolerance than the total white cell count, then the continuance of irradiation in these cases would almost certainly result in the production of a profound anaemia.

Comparison of the Platelet Count with the Lymphocyte Count.

The level of 300 lymphocytes per cubic millimetre (TOD) has been accepted as the safety level for purposes of comparison with the platelet count.

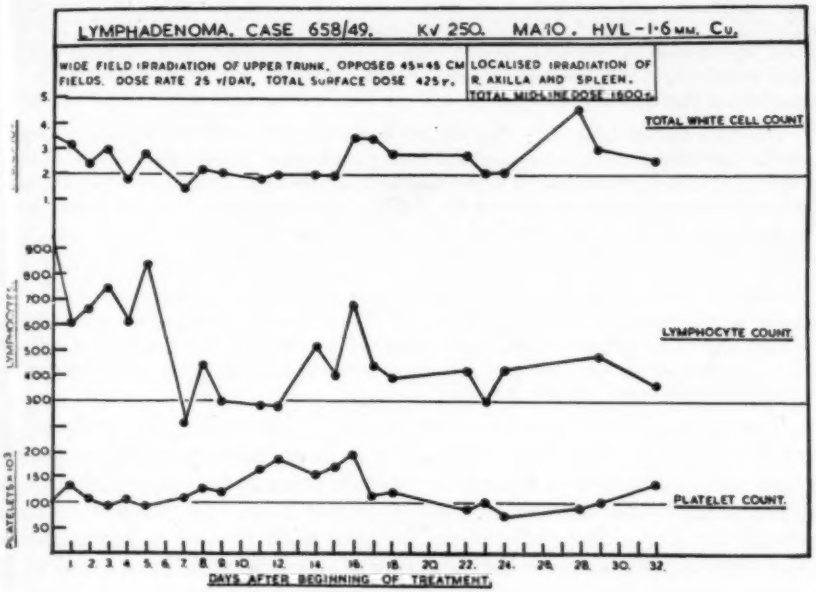

LYMPHADENOMA. CASE 658/49. KV 250. MA 10. HVL - 1·6 MM. Cu.
WIDE FIELD IRRADIATION OF UPPER TRUNK. OPPOSED 45×45 CM FIELDS. DOSE RATE 25 r/DAY. TOTAL SURFACE DOSE 425 r.
LOCALISED IRRADIATION OF R. AXILLA AND SPLEEN. TOTAL MIDLINE DOSE 1800 r.
TOTAL WHITE CELL COUNT
LYMPHOCYTE COUNT
PLATELET COUNT
DAYS AFTER BEGINNING OF TREATMENT

Fig. 17.

It has not been found that the lymphocyte count shows the constancy of response suggested by GOODFELLOW. While in some cases the curve of fall has been similar to that described by GOODFELLOW (Fig. 16 A), in others the count has shown a significant rise before the fall takes place (Fig. 16 B). These findings are in keeping with those of ELLIS who was unable to show any consistent pattern of response of the lymphocyte count under irradiation with roentgen rays. Similarly it has been found that radiation anaemia may supervene in a case when the lymphocyte level at the end of treatment was considerably above the safety level and conversely that irradiation is perfectly safe in the presence of a lymphocyte level below the safety level provided that the platelet count has not fallen below the level of 100,000 platelets per cubic millimetre.

Case No. 15,000: The patient was referred to the Radiotherapy Department in February 1942, suffering from mycosis fungoides. On 16. 2. 42 treatment was commenced, irradiation of the whole trunk by opposed anterior and posterior fields being undertaken. The technical factors were K. V. 250, Ma. 10, Half Value Layer, 1.6 mm. Cu. and incident dose rate on each field 20 r/day. On 23. 2. 42 the incident dose rate was increased to 30 r/day on each field. On 16. 3. 42 the patient developed petechial haemorrhages and treatment was stopped. The total white cell count was 5,000 cells per

cubic millimetre, and the lymphocyte count was 1,185 cells per cubic millimetre. The patient died on 28. 2. 42 from radiation anaemia and uncontrollable epistaxis. Note the actual appearance of petechial haemorrhages during treatment, and while no platelet count was done, it is quite safe to assume that the count was well below what is now regarded as the level of safety.

Case No 658/49 (*Fig. 17*): The patient was first referred to Radiotherapy Department in February 1949 an enlarged gland having been noted in the right axilla in January 1949. On examination there was a glandular mass in the right axilla measuring 10 cm. in diameter. Several glands were present in the left axilla measuring 2 cm. in diameter, and the lower pole of the spleen was palpable below the costal margin. The platelet count was 100,000 platelets per cubic millimetre, but it was felt that it might be possible to administer a worth while dose before the usual peak values had been replaced by a fall to the safety level. During treatment the lymphocyte count for a period of time was both on and below the safety level. Wide field irradiation was stopped when the platelet count fell again to 100,000 platelets per cubic millimetre, and the patient has since remained perfectly well without developing an anaemia in spite of the low level reached by the lymphocyte count during treatment.

The general conclusion can be reached that using the lymphocyte count to control wide field irradiation it is no more possible to predict which case will develop radiation anaemia than is the case with the use of the total white cell count. On the other hand the platelet count is superior to either form of control because with its use it is possible to identify during treatment the minority of cases in which the total white cell and lymphocyte counts fail as biological indicators.

The Practical Application of the Platelet Count

Two main groups of cases may be considered suitable for wide field irradiation:

(1) Those in which a cure can be effected — the very radiosensitive carcinomata and certain very radiosensitive types of reticulum cell sarcoma.

(2) Those in which the aim of treatment is palliation — the leukaemias, lymphadenoma, follicular reticulosis, and generalised aleukaemic reticulosis.

Our experience of malignant thymoma suggests that a proportion of these tumours may fall into the first group but that the majority fall into the second group.

In both groups observation of the pre-irradiation level of the platelet count and of its response during treatment, particularly its rate of fall, will yield valuable information for the guidance of treatment.

If the pre-irradiation level of the count is below 100,000 platelets per cubic millimetre the radiation tolerance of the case will be low, and it is not infrequent to find such cases in the second group, particularly those of chronic lymphatic leukaemia, aleukaemic leukaemia and aleuk-

aemic generalised reticulosis which are thus unsuitable for wide field treatment.

If the rate of fall of the platelet count is rapid, it will usually be found possible to modify this rate of fall in the first group of tumours by reducing the incident dose rate and if possible the size of fields irradiated. In this way the radiation tolerance of the individual is preserved, and it is possible for a curative dose to be given without the risk of development of a severe anaemia. In the second group, when a rapid fall of the platelet count occurs, it can be assumed that the case is an unsuitable one for wide field irradiation, which should then be modified to suitable localised treatment to enable the individual to have the maximum palliation with the minimum of risk of the development of a severe anaemia. This is particularly important in the wide field treatment of the chronic leukaemias. In these cases if the platelet count falls to the safety level before the total white cell count has reached the desired level then it is essential to stop wide field treatment no matter how high is the level of the total white cell count.

Appendix

The Technique used in Platelet Enumeration.

(1) After being cleaned with methylated ether, the dry skin of a finger is pricked and a red cell pipette, previously washed through with 3.8 % Sodium Citrate Solution, charged to the 1.0 mark.

(2) The pipette is then charged to the 1.01 mark with 3.8 % Sodium Citrate Solution, no dye being present in this solution.

(3) The pipette is shaken by hand for five minutes, or by a mechanical agitator.

(4) A red cell counting chamber is then charged in the usual way and placed in a Petri dish for ten minutes. The bottom of the Petri dish is lined with damp filter paper to prevent evaporation.

(5) On the immediate conclusion of this settling time of ten minutes the platelets are counted using a 1/6 objective.

(6) Using either a Thoma- or Neubauer-ruled counting chamber it is our practice to count all the platelets lying on the four intermediate sized squares forming one diagonal of the central double-ruled square, and also on one other intermediate square making five in all.

(7) Similar counts are done on two of the four peripheral large squares.

(8) The average value (N) for five of the smaller squares is then determined, and the count is given by the formula:

$$\frac{N}{2} \times 10{,}000.$$

It is important to observe rigidly the following points.

(1) The time at which a patient is treated during the day must be standardised.

(2) The time at which the count is performed in relation to the time at which the patient is treated must be standardised.

(3) One technician must do all the counts on one patient. Provided these variables can be effectively controlled it is possible to obtain consistent and accurate results with the technique described being used by haematological technicians employed on a whole time basis for this purpose.

It is important to remember that the safety level of 100,000 platelets per cubic millimetre only pertains to the technique described. If another technique is used it will be necessary to re-assess the value of the safety level.

Acknowledgements.

The author is indebted to Professor ROBERT MCWHIRTER and Professor L. S. P. DAVIDSON for their constant help and advice during the investigation. He is also indebted to Dr. C. A. MURISON, Physicist to the Radiotherapy Department, for various statistical calculations.

SUMMARY

Wide field roentgen treatment can be safely controlled by the observation of the platelet count.

The effect of wide field roentgen treatment on the platelet count is described both in cases with normal and abnormal haemopoiesis, and the relative merits of the platelet, lymphocyte and total white cell counts as biological indicators are discussed.

Experience has shown that in the majority of cases the total white cell count and the lymphocyte count are satisfactory indicators of when to terminate wide field roentgen treatment. In the minority, however, they do not act as satisfactory indicators and if reliance is placed on them a radiation anaemia will develop.

Observation of the basic principles described in the paper will enable the radiotherapist to undertake wide field irradiation in safety and with freedom of the risk of development of anaemia.

ZUSAMMENFASSUNG

Röntgentherapie mit grosser Behandlungsfläche lässt sich durch Beobachtung der Blutplättchenzahl in sicherer Weise kontrollieren.

Die Wirkung von Röntgenbehandlung mit grossem Behandlungsfelde auf die Plättchenzahl wird sowohl bei Fällen mit normaler als auch bei solchen mit abnormer Hämatopoese beschrieben und die relativen Vorzüge der Blutplättchenzahl, der Lymphozytenzahl und der Gesamtzahl weisser Blutkörperchen als biologische Indikatoren werden erörtert.

Die Erfahrung hat gezeigt, dass die Gesamtzahl der weissen Blutkörperchen und die Lymphozytenzahl in der Mehrzahl der Fälle genügende Indikatoren für die Abbrechung einer Röntgentherapie mit grossem Behandlungsfelde darstellen. Bei einer Minderzahl

von Fällen hindoch sind sie keine zuverlässigen Indikatoren, und wenn man sich auf sie verlässt, wird eine Strahlungsanämie zur Entwicklung kommen.

Beachtung der in dieser Arbeit beschriebenen Grundprinzipien wird es dem Radiotherapeuten ermöglichen, eine Grossfeldbestrahlung unter sicheren Verhältnissen und ohne die Gefahr der Entstehung einer Anämie durchzuführen.

RÉSUMÉ

La rœntgenthérapie par champs étendus peut être contrôlé sans danger par la numérotation répétée des plaquettes sanguines.

L'auteur expose l'effet de la rœntgenthérapie à grands champs sur le chiffre des plaquettes aussi bien dans les cas où l'hématopoièse est normale que dans ceux où elle est anormale, et il discute des mérites relatifs du compte des plaquettes, de celui des lymphocytes et du compte total des globules blancs en tant qu'indicateurs biologiques.

L'expérience a montré que dans la majorité des cas le compte total des globules blancs et celui des lymphocytes indiquent de façon satisfaisante à quel moment il convient d'arrêter le traitement rœntgenologique par champs étendus. Dans une minorité de cas, cependant, ces »indicateurs» sont trompeurs, et si l'on s'y fie on verra se développer une anémie due aux irradiations.

L'observation des principes fondamentaux décrits dans ce travail permettra au radiothérapeute d'entreprendre en sécurité l'irradiation par grands champs, sans s'exposer au risque de causer une anémie.

REFERENCES

Ellis, F.: Brit. J. Rad. XV: 194, 1942.
Goodfellow, D. R.: Acta Rad. XVII: 1, 1936.
Graham, J. M. and McWhirter, R.: Proc. Roy. Soc. Med. XL: 669, 1947.
Tod, M. C.: Proc. Roy. Soc. Med. XXXVII: 720, 1944.
Mossberg, H.: Acta Rad. XXVII: 400, 1946.
— Acta. Rad. XXVIII: 100, 1947.
— Acta. Rad. Suppl. LXVII: 1947.

FROM THE AKERSHUS COUNTY HOSPITAL ROENTGEN DEPARTMENT, OSLO, NORWAY
(HEAD: TORFINN DENSTAD; M. D.)

THE RESORPTION OF ABRODIL IN MYELOGRAPHY[1]

by

Torfinn Denstad

ARNELL, who together with LIDSTRÖM inaugurated this method of examination in 1931, states in his monograph on »Myelography with water-soluble contrast» (1948) that »a number of serious complications have occurred». He refers in this chiefly to an investigation carried out in 1945 by LINDBLOM: in 721 abrodil myelographies undertaken by Swedish radiologists complications occurred in more than 54 cases. We shall deal here only with some late complications: shock occurred in 8 cases after 1—3 hours, in 2 cases after 3—24 hours, and hyperaesthesia and latent spasms in 2 cases after 3 hours.

Since we started using abrodil myelography at The Akershus County Hospital in the autumn of 1946, we have performed 70 such examinations. We have applied the technique of ARNELL and LIDSTRÖM with LINDBLOM's modification of the projections. In two patients cramps occurred after approximately three hours, in the one quite slight and only in the upper extremities, in the second general clonic and tonic spasms with cyanosis, unconsciousness and tongue biting. The symptoms lasted only for about 10 minutes. A third patient collapsed a couple of hours after the examination, with barely perceptible pulse and superficial respiration. The attack passed after administration of stimulants. There was no fall in the blood pressure in any of the cases.

These complications must be supposed to be due to meningeal irritation released by the contrast medium — they can hardly be ascribed to the lumbar puncture or the spinal anaesthesia like the majority of minor complications which occasionally occur.

Previously we placed the patients — as usual after lumbar puncture (and spinal anaesthesia) — with lowered head of the bed during the twenty-four hours immediately following the examination. The complications which, as mentioned above, occurred a little late in the course,

[1] Read at the Meeting of the Northern Association for Medical Radiology, June 10—12, 1949; submitted for publication Aug. 25, 1949.

however, have made us doubt the sensibility of this. We are aware, of course, that abrodil (mono-iodo-methane sulphonate of sodium)[1] is strongly hypertonic, and that the endothelium of the subarachnoid space is very sensitive to physical and chemical effects (SÄKER). That is why we have to use lumbar anaesthesia (we have used parocain 0.10). Abrodil is resorbed quickly from the spinal fluid, though perhaps not quick enough to prevent that the heavy opaque substance — when the patients are placed with lowered head — reaches up to the cisterns and from here proceeds to the surface of the brain in a sufficient amount to release irritation phenomena.

In order to be able to arrive at a definite standpoint regarding this problem, we have in a few patients determined the abrodil content in the spinal fluid (calculated as dry substance) in the cisterna magna and in the lumbar region at different times after the injection and with the patients in different positions. We used for the myelography 10 ml 20 per cent abrodil (Kontrast »U» or Myelotrast).

Cisternal Punctures (Diagram I).

Lowered head (case nos. 1 and 2): 55 mins. and 1 hr. 25 mins. respectively after the injection of the contrast medium 0.82 per cent abrodil was found in both. Renewed puncture in case 2 after 3 hrs. 15 mins. demonstrated 0.55 per cent.

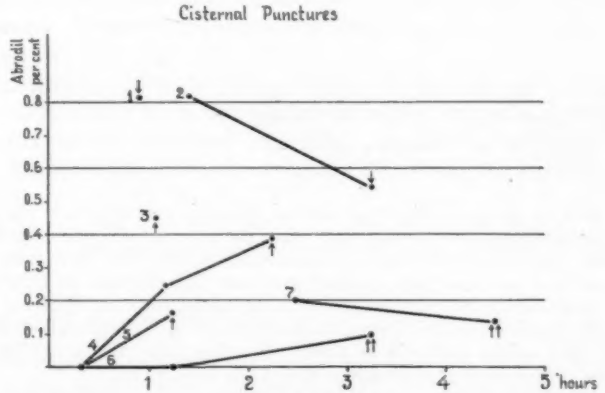


Diagram I. The abrodil concentration in cisterna magna at different times after the myelography and with the patients in different positions: lowered head (↓), raised head (↑) and seated in bed (↑↑).

[1] For the sake of simplicity we use the designation abrodil all the time, even if at first we applied the Swedish medium kontrast »U» (Leo) and later the Norwegian medium Myelotrast (A. L.).

FROM THE AKERSHUS COUNTY HOSPITAL ROENTGEN DEPARTMENT, OSLO, NORWAY
(HEAD: TORFINN DENSTAD; M. D.)

THE RESORPTION OF ABRODIL IN MYELOGRAPHY[1]

by

Torfinn Denstad

ARNELL, who together with LIDSTRÖM inaugurated this method of examination in 1931, states in his monograph on »Myelography with water-soluble contrast» (1948) that »a number of serious complications have occurred». He refers in this chiefly to an investigation carried out in 1945 by LINDBLOM: in 721 abrodil myelographies undertaken by Swedish radiologists complications occurred in more than 54 cases. We shall deal here only with some late complications: shock occurred in 8 cases after 1—3 hours, in 2 cases after 3—24 hours, and hyperaesthesia and latent spasms in 2 cases after 3 hours.

Since we started using abrodil myelography at The Akershus County Hospital in the autumn of 1946, we have performed 70 such examinations. We have applied the technique of ARNELL and LIDSTRÖM with LINDBLOM's modification of the projections. In two patients cramps occurred after approximately three hours, in the one quite slight and only in the upper extremities, in the second general clonic and tonic spasms with cyanosis, unconsciousness and tongue biting. The symptoms lasted only for about 10 minutes. A third patient collapsed a couple of hours after the examination, with barely perceptible pulse and superficial respiration. The attack passed after administration of stimulants. There was no fall in the blood pressure in any of the cases.

These complications must be supposed to be due to meningeal irritation released by the contrast medium — they can hardly be ascribed to the lumbar puncture or the spinal anaesthesia like the majority of minor complications which occasionally occur.

Previously we placed the patients — as usual after lumbar puncture (and spinal anaesthesia) — with lowered head of the bed during the twenty-four hours immediately following the examination. The complications which, as mentioned above, occurred a little late in the course,

[1] Read at the Meeting of the Northern Association for Medical Radiology, June 10—12, 1949; submitted for publication Aug. 25, 1949.

however, have made us doubt the sensibility of this. We are aware, of course, that abrodil (mono-iodo-methane sulphonate of sodium)[1] is strongly hypertonic, and that the endothelium of the subarachnoid space is very sensitive to physical and chemical effects (SÄKER). That is why we have to use lumbar anaesthesia (we have used parocain 0.10). Abrodil is resorbed quickly from the spinal fluid, though perhaps not quick enough to prevent that the heavy opaque substance — when the patients are placed with lowered head — reaches up to the cisterns and from here proceeds to the surface of the brain in a sufficient amount to release irritation phenomena.

In order to be able to arrive at a definite standpoint regarding this problem, we have in a few patients determined the abrodil content in the spinal fluid (calculated as dry substance) in the cisterna magna and in the lumbar region at different times after the injection and with the patients in different positions. We used for the myelography 10 ml 20 per cent abrodil (Kontrast »U» or Myelotrast).

Cisternal Punctures (Diagram I).

Lowered head (case nos. 1 and 2): 55 mins. and 1 hr. 25 mins. respectively after the injection of the contrast medium 0.82 per cent abrodil was found in both. Renewed puncture in case 2 after 3 hrs. 15 mins. demonstrated 0.55 per cent.

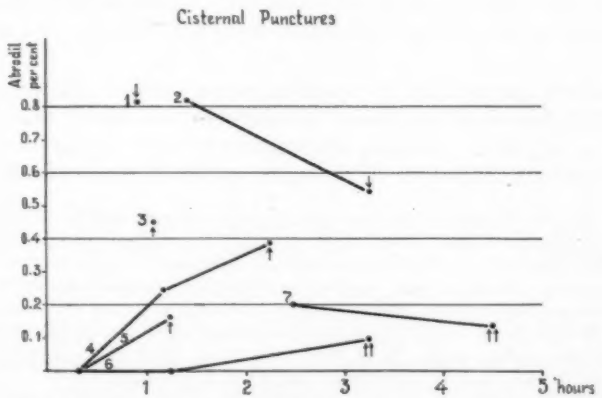


Diagram I. The abrodil concentration in cisterna magna at different times after the myelography and with the patients in different positions: lowered head (↓), raised head (↑) and seated in bed (↑↑).

[1] For the sake of simplicity we use the designation abrodil all the time, even if at first we applied the Swedish medium kontrast »U» (Leo) and later the Norwegian medium Myelotrast (A. L.).

Raised head (case nos. 3, 4 and 5): In two patients (case nos. 4 and 5) the cisternal fluid was examined 20 mins. afterwards without any abrodil being demonstrable here. After 1 hr. 5 mins., 1 hr. 10 mins., and 1 hr. 15 mins., 0.45 per cent, 0.25 per cent and 0.16 per cent was found in case nos. 3, 4 and 5 respectively. In case 4 puncture was carried out also after 2 hrs. 15 mins., demonstrating continued increase in concentration, viz. 0.39 per cent.

Seated in bed (case nos. 6 and 7): In case 6 no abrodil was demonstrable in the cisternal fluid after 20 mins. and after 1 hr. 15 mins. After 3 hrs. 15 mins., however, 0.10 per cent was found, and in case 7 0.20 per cent was found after 2 hrs. 30 mins. and 0.14 per cent even after 4 hrs. 30 mins.

Thus, it is obvious that when the patients after the examination are placed with raised head (wooden blocks 10 cm high), the content of contrast substance in the cisternal fluid is considerably lower than when they are lying with lowered head. This is no more than could be anticipated, it is only surprising that the difference is no greater. The capability of the opaque medium to diffuse against gravity, therefore, must be rather great. Other factors, of course, must also be taken into account. As demonstrated by REITAN the subarachnoid space will be narrowed if the patients use pressure, whereby some of the lumbar fluid, which is richer in contrast substance, is forced upwards into the thoracic region. Perhaps this may also explain the varying concentration of the opaque medium in different patients at approximately the same point of time.

Even when the patient is seated in bed after the examination, some opaque substance may be found in the cisternal fluid even 4½ hours after the injection of abrodil, although probably somewhat less than when the patient is placed in ordinary position with raised head.

With a view to the possibility that abrodil, which is resorbed from the lumbar fluid while the concentration here is still high, may perhaps return again further cranially into the spinal fluid which contains no contrast substance, and thus contribute to the increase of contrast medium here, lumbar puncture was carried out in two patients 2 and 3 hours respectively after urography with 20 ml 35 per cent Urotrast »Nyco» (*i. e.* perabrodil (diethanol-amino-dijod-pyridon-N-acetate)). No opaque substance was demonstrable in the spinal fluid. It is likely, therefore, that the possibility mentioned above may be disregarded also as far as abrodil is concerned.

Even if the amounts of opaque substance in the cisternal fluid are small after abrodil myelography, they are still sufficiently large — particularly when the head is lowered — that it may be easily imagined that irritation phenomena may be released on the part of the meninges. If we accept this possibility, the following question presents

itself: What can we do to prevent the diffusion of the abrodil in cerebral direction?

There are two routes of approach:

We can place the patient with the head raised during the first 4—5 hours after the examination or, if this does not prove satisfactory, on a back rest. This precaution is contrary to the common rule, however, that patients after lumbar puncture and anaesthesia shall be placed with the head low in order to prevent as much as possible leakage through the puncture opening and consequently reduced pressure in the spinal fluid, which in its turn caused headache. This theory has not been accepted by all investigators, however (THORSÉN, NYGAARD, a. o.). Thus NYGAARD found that 73 patients operated on for gangrenous appendicitis under spinal anaesthesia, and placed in Fowler's position, therefore, did not develop headache more frequently than those who were placed with the head low. Cardiovascular collapse occurred in no cases. If a thin puncture needle is used ($^1/_2$—$^3/_4$ mm diameter), there should be reason to believe that the positioning does not play such an important part. In any case one has to choose the lesser of two evils, and it appears reasonable then that the effects aimed at preventing the contrast medium from wandering rostrally should weigh the heaviest.

If this procedure still should result in an increase in the number of complications in the form of headache and perhaps cardiovascular collapse, there is also another route to be resorted to. It should be endeavoured to aspirate as much as possible of the abrodil by a fresh lumbar puncture just after the examination. The lumbar part of the subarachnoid space contains up to about 10 ml spinal fluid (ARNELL). If 15—20 ml are aspirated, therefore, and replaced by physiological saline solution, it should be possible to remove the greater part of the still unresorbed opaque medium. LINDBLOM has done this on some occasions, but has given up the method as he did not observe any useful effect. The author has examined the abrodil concentration in the lumbar fluid in a few cases in order to get an idea of how much abrodil may be removed in this way:

Lumbar Punctures (Diagram II — scale 1/10 of scale in Diagram I).

In three patients (case nos. 4, 6 and 5) 9.20, 6.60 and 5.17 per cent abrodil respectively were demonstrated 15—25 minutes after the injection. Thus, the quantity has already been reduced to one half or one quarter of the original concentration (20 per cent). Only 1—2 ml was aspirated for the examination. In case 5 the lumbar fluid was examined also after 1 hr. 10 mins., when the concentration had fallen to 2.58 per cent. (The patient was lying with raised head.)

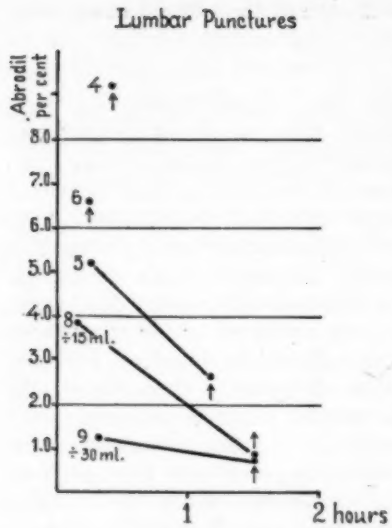


Diagram II. The abrodil concentration in the lumbar fluid at different times after the myelography without and with aspiration of spinal fluid containing opaque medium immediately after the examination. Raised head.

In two patients (case nos. 8 and 9) we then endeavoured to empty out some of the lumbar fluid containing opaque medium.

In case 8 we tapped 15 ml spinal fluid with a concentration of 3.78 per cent abrodil, corresponding to 2.8 ml 20 per cent abrodil.

In case 9 30 ml spinal fluid was tapped with a concentration of 1.25 per cent abrodil, corresponding to about 2 ml 20 per cent.

When we find such low concentration in these two as compared with the remaining cases, this is due to the fact that so much fluid is evacuated, resulting in greater dilution.

After 1 hr. 30 mins. an abrodil concentration was found in these cases of 0.84 per cent and 0.72 per cent respectively. (The patients were lying with the head raised.) This means, therefore, about the same concentration that we found in the cisternal fluid after about one hour in case nos. 1 and 2, which were lying with lowered head.

It is probable that no great risk is taken if these patients, in whom as much as possible of the not yet resorbed abrodil has been removed, are placed with lowered head immediately after the examination. We have tried this in two patients (case nos. 10 and 11, omitted in the diagrams), and determined the abrodil concentration in the cisternal fluid after 75 mins. and after 3 hrs.

In case 10 we tapped 20 ml spinal fluid by lumbar puncture with a concentration of 1.19 per cent abrodil, corresponding to 1.2 ml 20 per cent abrodil. After 75 mins. 0.05 per cent abrodil was found in the cisternal fluid, and after 3 hrs. traces only.

In case 11 we also tapped 20 ml lumbar fluid, with an abrodil concentration of 3.48 per cent, corresponding to 3.5 ml 20 per cent abrodil. After 75 mins. no abrodil was demonstrable in the cisternal fluid.

This is a remarkable difference from the high values found in the cisternal fluid in case nos. 1 and 2 (diagram I), which also were placed

with lowered head, but without preceding aspiration of the lumbar fluid containing opaque medium.

SUMMARY

Several hours after myelography with abrodil cisterna magna contains abrodil, particularly when the patients after the examination are placed with lowered head, to a lesser degree if they are placed with the head raised. The author holds the opinion that some complications, especially spasms and perhaps also collapse, which may occur after 2—3 hours, may depend on this migration in cephalic direction of the opaque medium. It is recommended that the patients be placed with raised head during the first 4—5 hours following the examination. If this procedure is not desirable due to the lumbar puncture carried out, about 20 ml of spinal fluid containing opaque medium should be tapped by a fresh lumbar puncture immediately after the examination and replaced with physiological saline solution. In this way an amount of opaque medium is removed corresponding to 2—4 ml 20 per cent abrodil and practically no opaque medium reaches the cisterna magna in spite of the patients being placed with lowered head.

ZUSAMMENFASSUNG

Mehrere Stunden nach Myelographie mit Abrodil kann Abrodil in Cisterna magna nachgewiesen werden, besonders wenn der Patient nach der Untersuchung mit gesenktem Kopf, aber auch, obwohl im geringerem Grade, wenn er mit erhöhtem Kopf gelagert wird. Der Verfasser vertritt die Meinung dass gewisse Komplikationen, insbesondere Krämpfe und vielleicht auch Kollaps, die nach 2—3 Stunden auftreten können, auf dieser Kontrastwanderung in cephaler Richtung zurückzuführen sind, und empfiehlt dass der Patient die ersten 4—5 Stunden nach der Untersuchung mit erhöhtem Kopf gelagert wird. Wünscht man wegen der ausgeführten Lumbalpunktion dieses Verfahren zu vermeiden, kan man etwa 20 ml der kontrasthaltigen Flüssigkeit mittels einer neuen Lumbalpunktion gleich nach der Untersuchung entfernen, und diese mit physiologischer Kochsalzlösung ersetzen. Dabei wird eine 2—4 ml 20 % Abrodil äquivalenten Kontrastmenge entfernt, und es gelangt nur ganz minimale Mengen Kontrast in die Cisterneflüssigkeit hinauf, selbst wenn der Patient mit gesenktem Kopf gelagert wird.

RÉSUMÉ

On peut démontrer la présence de la substance opaque de contraste dans la grande cisterne plusieurs heures après une myelographie à l'Abrodil, surtout si les malades ont été placés la tête basse, dans un degré beaucoup plus faible si la tête a été surélevée après l'examen. Cette migration du contraste en direction céphalique pourrait être responsable, à l'avis de l'auteur, de certaines complications, particulièrement de crampes et peut-être aussi des états de collapse, qui peuvent apparaître 2—3 heures après l'examen, et il recommande de placer les malades la tête surélevée les 4—5 premières heures après la myélographie. Si on hésitait de procéder ainsi à cause de la ponction lombaire qui venait d'être pratiquée, il faudrait retirer par une nouvelle ponction lombaire, faite immédiatement après l'examen, environs 20 cm³ de liquide céphalo-rachidien contenant la substance de contraste, que l'on remplace par du sérum salé physiologique. De cette manière on évacue une quantité de contraste correspondant à 2—4 cm³ d'Abrodil à 20 %, ainsi il n'arrivera pratiquement pas de substance de contraste dans la cisterne, même si les malades par la suite seraient placés la tête basse.

REFERENCES

ARNELL, S. & LIDSTRÖM: Acta rad. 1931, 12, 287.
ARNELL, S.: Myelography with water-soluble contrast. Acta rad., suppl. LXXV. Stockholm 1948.
LINDBLOM, K.: Acta rad. 1946, 27, 1.
— Acta rad. 1947, 28, 69.
NYGAARD, K. K.: Acta chir. scand. 1936, 78, 379.
REITAN, H.: Acta rad. 1941, 22, 762.
SÄKER, G.: Klin. Wo. 1940, 19, 780 (quoted in Nordisk Medicin).
THORSÉN, G.: Nordisk Medicin 1942, 16, 3577.

FROM THE ANATOMICAL INSTITUTE, UNIVERSITY OF OSLO, NORWAY.

THE DEVELOPMENTAL ANATOMY OF THE PYLORIC CANAL AND THE ETIOLOGY OF INFANTILE PYLORIC STENOSIS[1]

by

Johan Torgersen, M. D.

The pyloric sulcus has an asymmetrical position in relationship to the axis of the transverse stomach. It is closer to the angulus on the lesser curvature side. The circular fibres of the muscular layer radiate like a fan from the lesser curvature side, embracing the greater curvature. This structure is an expression of the asymmetry of the stomach regarding structure and topography. In some species is found a mucous membrane torus on the lesser curvature side. The relationship between the thickness of the musculature and the mucous membrane on the lesser curvature side accord with regular rules. If the musculature is thin a mucous membrane torus is present. If the musculature is thick as in man, no mucous membrane torus is present except functionally.

The asymmetry of the muscular structure of the pyloric canal has a relationship to the topographical asymmetry. This fact makes the relationship of the stomach to the asymmetry of the viscera essential to an understanding of the abnormalities in the anatomy of the pyloric canal. The differentiation of the musculature and the mucosal pattern depends on the place of the stomach in development. This supposition is in conformity with the statement of the experimental embryologists that the final shape and structure of a part of the organism depend on the place of that part in development, particularly on the relationship to the main axes of the body. For this reason the causative factors in the asymmetry of the viscera may be supposed to be fundamental in the normal and abnormal development of the pyloric canal.

The pyloric canal is particularly long in infantile pyloric stenosis. The transverse stomach is mostly relatively short. A true angulus may

[1] Submitted for publication Sept. 8, 1949.

be absent. The region between the angulus and the pyloric sulcus has apparently been impeded in the growth in length. The distal part, the pyloric canal, has increased in thickness at the expense of the growth in length of the transverse stomach (Fig. 1).

It is evident that an hereditary malformation is one of the factors in the disease. Whether the radiological findings are present before the onset of the symptoms or not is irrelevant. An hereditary disease may manifest itself in different ages. The disease is relatively frequent in boys and in children who tend to be taller than the average when examined as grown ups (RINVIK, 1940, SALMI, 1941). The attempts so far to interpret the data concerning familial occurrence by a single gene have not been successful. (PENROSE and COCKAYNE, 1943.)

In the studies of partial inversion, PERNKOPF reports three cases of isolated inversion of the stomach. Two of them showed no differentiation of the musculature or the mucosa of the pyloric canal which looked like the small intestine (Figs. 1 and 2). These cases represent a counterpoint to the infantile pyloric stenosis (Fig. 1). The transverse stomach and the pyloric canal have in these cases apparently grown in length without any restraint and at the expense of the growth in thickness. The third case showed and inverse stomach and a duodenum in the normal situs (Fig. 1). For this reason there was a sharp angle at the transition from the stomach to the duodenum. The musculature of the pyloric canal was thick as in infantile pyloric stenosis. The pyloric canal has apparently been impeded in growth along the axis of the transverse stomach. In case of the infantile pyloric stenosis a corresponding restraint with regard to the growth along this axis may be supposed to be due to an abnormally asymmetrical position of the pyloric canal depending on an excessive degree of rotation of the stomach.

The differentiation of the pyloric canal depends on the factors in the asymmetry of the viscera, therefore. In a previous study the author has made an approach to the genetics of the asymmetry of the viscera (1949). The most reasonable interpretation of the observations was that the asymmetry of the viscera depends on a complex of genes which may be broken up in components concerned with the development of the particular organs. This complex of genes may be supposed to condition the manifestation of the genes affecting the development of the stomach in infantile pyloric stenosis. There is good evidence that the genic factors in the asymmetry of the viscera and the genic factors in sex and stature are integrated. This integrative action of the genes manifests itself in the excessive asymmetry supposed to be the cause of the abnormality of the stomach, in the sex ratio in the disease and in the bodybuild of these children.

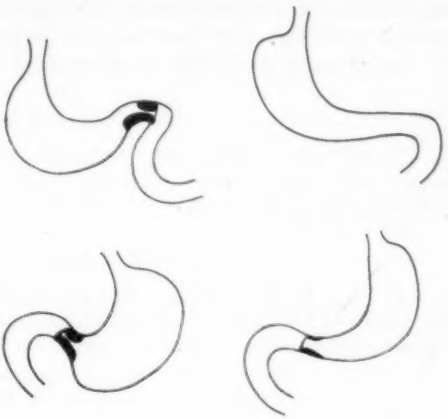


Fig. 1. Upper left, the pyloric canal in isolated inversion of the stomach and normal situs of the duodenum. Upper right, in isolated inversion of both stomach and duodenum. Lower left, in infantile pyloric stenosis. Lower right, in the normal stomach.

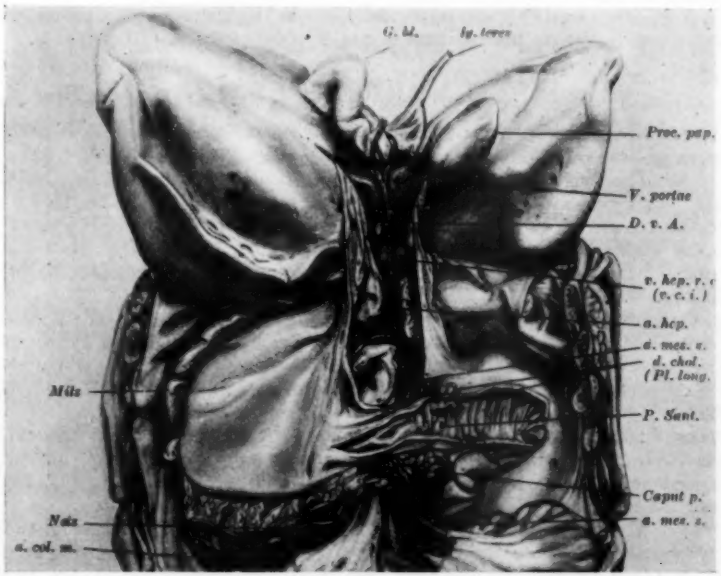


Fig. 2. From PERNKOPF, 1926. The pyloric canal in isolated inversion of the stomach.

The present paper does not intend to give a comprehensive representation of the controversial theories concerning the etiology of infantile pyloric stenosis. The intention is to report observations which indicate an important, probably fundamental factor in the disease.

SUMMARY

On the basis of the anatomy of the pyloric canal in infantile pyloric stenosis, in the normal situs and in cases of isolated inversion of the stomach is dealt with the part played by the genic factors in visceral asymmetry in the disease.

ZUSAMMENFASSUNG

An Hand der Anatomie des Pyloruskanals bei Pylorusstenose des Kindes, bei normalem Situs und bei Fällen von isolierter Inversion des Magens, wird die Rolle genetischer Faktoren für viszerale Asymmetrien bei dieser Krankheit besprochen.

RÉSUMÉ

C'est sur la base de l'anatomie au canal pylorique dans la sténose infantile, aussi bien lorsque les organes sont dans leur position normale que dans les cas de situs inversus limité à l'estomac, que l'auteur traite du rôle que les facteurs d'asymétrie viscérale représentés par les gènes jouent dans la maladie en question.

REFERENCES

Cockayne, E. and Penrose, L.: The genetics of congenital pyloric stenosis. The Ohio Journ. of Science. 43, 1943.

Cole, L. G.: The living stomach and its motor phenomenon. Acta Rad. 9, 533, 1928.

Forssell, G.: Pylorospasmens patogenes. Svenska Läk.sällsk. förh. 78, 1932.

Frimann-Dahl, J.: Über den Nachweis der sogenannten kongenitalen Pylorushypertrophie durch Röntgenuntersuchung. Acta Rad. 16, 333, 1935.

Pernkopf, E.: Der partielle Situs inversus der Eingeweide beim Menschen. Zschr. Anat. u. Entw. G. 79, 577, 1926. Ibid. 87, 661, 1928.

Rinvik, R.: Investigations of congenital stenosis of the Pylorus. Acta Pæd. 27, 296, 1940.

Runström, G.: On the Roentgen-anatomical Appearance of Congenital Pyloric Stenosis during and after the Manifest Stage of the Disease. Acta Pæd. 26, 383, 1939.

Salmi, T.: Untersuchungen über den Pylorospasmus der Säuglinge. Acta Pæd. 28, 270, 1941.

Torgersen, J.: The muscular Build and Movements of the Stomach and duodenal Bulb. Acta Rad. Suppl. 95, 1942.

— Concordant Situs inversus in dizygotic twins. Journ. Heredity. 39, 293, 1948.

— Genic factors in visceral asymmetry. Arch. Pathol. 47, 566, 1949.

Wernstedt, W.: Zur Frage der Anatomie und der Motorik des Pylorusmundstücks und des Magenmotors im normalen und pylorospastischen Säuglingsmagen. Acta Pæd. 31, 73, 1943—1944.

— Zur Kenntnis der Form des angulopyloralen Querfortsatzes (Querstücks) des kindlichen Magens und dessen Ringmuskulatur. Acta Pæd. 1944, Suppl. 1, 32, 791.

AUS DER RÖNTGENABTEILUNG (CHEF: MED. DR. SIGFRID ARNELL) DES CENTRAL-LAZARETTES IN GÄVLE, SCHWEDEN.

LIPOCHONDRODYSTROPHIE (HURLER'S SYNDROM)[1]

von

Gustaf Notter

Mit Hurler's Syndrom bezeichnet man einen unproportionierten Zwergwuchs mit allgemeiner Chondrodystrophie, typischen symmetrischen Skelettveränderungen, Hepatosplenomegalie, mangelhafter geistiger Entwicklung und Corneatrübungen als Kardinalsymptomen. Die Ätiologie des Leidens ist noch unklar, wenn auch die Mehrzahl der Autoren eine Störung des Lipoidstoffwechsels für die Ursache hält. Das Krankheitsbild wurde im Laufe der Jahre mit mehreren Namen versehen, wie Hurler's Syndrom, Gargoylismus,[2] Dysostosis multiplex, Chondro-osteodystrophie und Lipochondrodystrophie. Auch wurden im Anfang nahe verwandte Bilder wie Morbus Morquio, Typus E, u. a. mit ihm identifiziert. Erst in den letzten Jahren gelang es allmählich die charakteristischen Symptome zu bestimmten Krankheitsbildern zusammenzufassen. Ob endgültig, muss solange dahingestellt bleiben, wie Ätiologie und Pathogenese noch nicht restlos bekannt sind.

Literatur

Die ersten beiden Fälle wurden 1919 von GERTRUD HURLER (1) aus der Münchener Universitätskinderklinik beschrieben und als Sonderfälle ossaler und kartilaginärer Dystrophie den bereits bekannten 3 Gruppen: dystrophia periostalis hyperplastica, cranio-facialis und cleido-cranialis zur Seite gestellt. 1920 berichtet PFAUNDLER (2) über die gleichen Fälle, weshalb man auch von Hurler-Pfaundler Syndrom spricht. 1921 beschrieben JEWESBURY and SPENCE (50) 2 Chondrodystrophie-Fälle ohne die typischen Merkmale des Hurlerschen Syndroms. 1929 veröffentlichte BAILSFORD (4) einen Fall von »Chondro-osteodystrophie», der einem 1926

[1] Bei der Red. am 24. VIII. 1949 eingegangen.

[2] Hergeleitet von den grotesken, teils drachenförmigen Wasserspeiern an den Dächern gotischer Dome, mit denen das Gesicht des Pat. verglichen wird.

von SILVERSKJÖLD beschriebenen Fall gleichen soll. 1929 MORQUIO (3) »une forme de dystrophie osseuse familiale». Lange Zeit hielt man Hurler's und Morquio's Syndrom für identisch, jedoch zeigten diese Fälle (4, 11, 6, 20 u. a.) keine Schädeldeformitäten, Intelligensdefekte und Corneatrübungen und werden heute als besondere Krankheitsbilder angesehen. 1931 stellte RUGGLES (7) 3 Fälle vor, von denen 2 klare Gargoylismus-Fälle waren. HARRINGTON und HELMHOLTZ (erwähnt bei 25) sahen 4 Fälle. Weitere Fälle beschrieben BINSWANGER und ULLRICH (28), POYNTON-LIGHTWOOD-ELLIS (36), SHELDON (37), COCKAYNE (31 + 32), ELLIS-SHELDON-CAPON (14), NORDMANN (35), ASHBY-STEWART-WATKIN (12), TEN BOKKEL HUININK (30), LIEBENAM (33), ELLIS (15—17), SLOT-BURGESS (38), BESDZIEK (27), BINDSCHEDLER (29), KRESSLER-AEGERTER (9), BERLINER (26), ENGEL (23), MEYER-OKNER (34), JEWESBURY-SPENCE (50), MEYER-BRENNEMANN (6), LARSON-LICHTY (21). HARVEY (25) zählte 1942 38 sichere Fälle, HENDERSON (52) 1940 bereits 57 und fügte 5 eigene hinzu.

Die Angaben der Literatur sind also auseinandergehend, was sicher beruht auf der ungenauen Abgrenzung mancher Fälle gegenüber dem von HURLER geschilderten Syndrom.

1942 beschrieb DE LANGE (43 + 44) 2 Fälle eines »Typus E», der von einigen Forschern mit Hurler's Syndrom identifiziert wurde. Seit 1943 sind eine Reihe weiterer Fälle berichtet worden, die aber die Pathogenese ebenfalls nicht aufklären konnten.

Die *klinischen* Erscheinungen sind so charakteristisch, dass die Diagnose schon nach dem Äusseren des Pat. gestellt werden kann. Ein unproportionierter Zwergwuchs mit kurzem Rumpf, Extremitäten und Nacken, grossem Kopf, groteskem Gesicht, eingesunkenem Nasenrücken, prominenten Supraorbitalkanten, tiefsitzenden Ohren, plumpen Augenbrauen, dicken Lippen, fleischiger dicker Zunge, die oft zwischen den geöffneten Lippen liegt, verzögerter Dentition, schadhaften, schlecht entwickelten Zähnen und weiten unregelmässigen Zahnlücken. Der Brustkorb ist vorgewölbt, der Bauch dick, häufig Umbilical- oder Inguinalhernie. Hepatosplenomegalie. Lumbalkyphose im Bereich Th_{12}—L_2. Beine und Arme in schwacher Flexion leicht fixiert. Extreme Flexion und Extension unmöglich. Interdigitalgelenke ebenfalls leicht flektiert und fixiert, sodass Faustschluss nicht möglich ist. Schlappe Muskulatur. Coxa valga, genu valgum. Breite kurze Hände und Füsse, oft geschwollen wie bei Rachitis. Asymmetrischer Turm- oder Langschädel, Hydrocephalus internus, meist aber Scaphocephalus mit ausladenden Stirn- und Schläfenbeinen. Hypertelorismus. Mangelhafte Pneumatisation des Schädels. Corneatrübungen. Otosklerose. Adenoide und mucopurulente Rhinitis. Lanugobehaarung auf Schulter, Armen und Rücken. Verzögert

Geschlechtsreife beim männlichen Geschlecht, keine Zeugungsfähigkeit beim weiblichen Geschlecht. Mangelhafte geistige Entwicklung. Psyche nur teilweise verändert. Die Laboratoriumsbefunde sind normal ausser einer in manchen Fällen beobachteten Hypercholesterinämie.

Röntgenologisch ist der Skelettbefund typisch und sollte, auch bei der relativen Seltenheit des Krankheitsbildes dem Röntgenologen bekannt sein. Die typische Lumballordose im Bereich Th_{12}—L_2, die den Eltern erst auffällt wenn das Kind zu sitzen oder laufen beginnt und wegen der das Kind meist erstmalig in Behandlung kommt, unterscheidet sich deutlich von der einer spondylosis tuberculosa, morbus Scheuermann, aber auch von den Lordosen anderer Lipoidosen wie Hand-Schüller-Christian (H—S) und Gaucher. H—S beruht auf einer Störung des Cholesterinstoffwechsels, ev. mit erhöhten Cholesterinwerten, typischen Defekten an Schädel, Becken, Gliedmassen und Wirbelsäule, kombiniert mit Exophthalmus und diabetes insipidus. Mb. Gaucher beruht auf einer Cerebrosidspeicherung mit Hepatomegalie, Pigmentierung, Anaemie und Kachexie. Bei Hand-Schüller-Christian sind mehrere Wirbel befallen. Diese sind ungleich hoch und teils osteoklastisch, teils sklerotisch umgebaut. Dagegen besteht beim Gaucher meist ein umschriebener Gibbus durch Zerstörung eines oder mehrerer Wirbel in spitzer Keilform. Beide Krankheiten befallen meist eine normal ausgebildete Wirbelsäule, während beim Typus Hurler eine ausgesprochene Wachstumshemmung zum Gibbus führt. In allen Fällen ist die Veränderung am Übergang des Thorakal- und Lumbal-Abschnittes lokalisiert und betrifft meist 2 Wirbel. Diese sind kleiner, nach hinten verschoben und weisen an der ventralen kranialen Kante einen abgerundeten Defekt auf. Die nahezu normalgrosse Wirbelbasis tritt hakenförmig vor, sodass man in ausgeprägten Fällen an die Form eines dorsalen Halbwirbels erinnert wird. Man kann mit BRAILSFORD (4) darin übereinstimmen, dass die Kyphose als kombinierte Folge einer Entwicklungshemmung und statischer Überbeanspruchung infolge verzögerter Ausbildung der Gelenkfortsätze entsteht. Aber auch die benachbarten Wirbel weisen annähernde Veränderungen auf. Allgemein ist die Verkalkung der Wirbelbogenepiphysen und der Quer- und Dornfortsätze verzögert. Die Intervertebralscheiben sind dagegen unverändert, was eines der wichtigsten Merkmale gegenüber allen degenerativen und entzündlichen Veränderungen ist. Niemals sieht man Abszesschatten. Die Rippen sind breit und riemenförmig und verjüngen sich in ihrem vertebralen Ende. Die Schlüsselbeine sind verlängert und an ihrem sternalen Ende plump und verdickt. Die Schulterblätter stehen hoch und sind klumpig. Die Beckenepiphysen sind weit. Die Verschmelzung der Sacralwirbel erfolgt sehr verzögert. Die Hüftgelenkspfannen sind flach und kaum ausgebildet, die Epiphysenkerne des caput femoris

klein, ausgeprägte coxa valga und genu valgum, im Kniegelenk oft freie Körper. Doch sind die Veränderungen an den unteren Extremitäten weniger stark ausgeprägt als den Armen. Die Röhrenknochen sind kurz und plump, ähnlich denen des Chondrodystrophikers. An Muskelansätzen und cristae interosseae finden sich manchmal periostale Verdickungen. Der Radius ist distal länger als die Ulna. Die Epiphysen sind verbreitert und gegeneinander spitz ausgezogen, die Kerne oft gedoppelt. Die Gelenkflächen stehen in einem Winkel von cirka 135° zueinander und sind distal-konvex wellenförmig deformiert, aber scharf begrenzt, ungefähr wie bei einer ausgeheilten Rachitis. Auch fehlen nicht die für diese so typischen »Jahresringe». Carpal- und Tarsalknochen sind in der Entwicklung weit zurück, Metacarpalia und -tarsalia breit, klumpig, mit spitzen Basen, dünner Corticalis, grobmaschiger, rarefizierter Spongiosastruktur von beinahe schwammartigem Aussehen. Interphalangealgelenke stehen in leichter Flexion.

Der Schädel ist meistens deformiert im Sinne eines Scaphocephalus mit ausladenden Stirn-, Scheitel- und Temporalbeinen. Auch Plagio-, Acro- und Dolichocephalus wurden beobachtet. Die sutura coronalis und squamalis klaffen. Die excavatio hypophysea ist langgestreckt und flach. Die processus clinoidei sind oft unregelmässig geformt, die sella aber immer unbeschädigt. Mangelhafte Pneumatisation der sinus und Warzenfortsätze. Ober- und Unterkiefer sind prominent. Exostosen an der Schädelbasis sind beschrieben. Keine knochenzerstörenden, kariösen Prozesse. Die Kalotte ist dünn, deutliche Gefässzeichnung.

Patologisch fanden sich, entsprechend den verschiedenen Krankheitsgruppen, auch unterschiedliche Veränderungen. So fanden Ashby-Stewart-Watkin (12), deren Fall keine Milz- und Leberschwellung aufwies, auch keine Lipoidablagerung im Reticuloendothelialsystem und keine Schaumzellen. Die Ganglienzellen hatten verändertes Cytoplasma, die Nissel'schen Schollen waren vermindert, zu einem Häufchen zusammengedrängt und der nur wenig geschädigte Kern stand am Rande. Washington (22), der 6 Fälle untersuchte, fand Cytoplasmalipoide im Hirnstamm und in den Basalganglien, peri- und extracellulär. Er hielt dieses für Cerebrosid, führte aber keine genaue biochemische Bestimmung durch. Ebenfalls fand sich Lipoid in Leber, Milz, Lymphknoten, Lunge, Herz und Thymus. Er vertrat daher die Verwandschaft des Hurler-Syndroms mit den Lipoidosen und schlug den pathogenetischen Namen Lipochondrodystrophie vor. Auch Ellis und Sheldon (14) und Larson (21) vertreten diese Ansicht, während de Rudder (49) Hurler's, Morquio's Syndrom und die Lipoidosen für Varianten einer Phosphatid-Diathese hält, denen die Hepato-splenomegalie gemeinsam ist. Kny (48) bält die amaurotische Idiotie (Tay-Sachs) und Hurle 's

Syndrom für identisch. Er fand ausserdem Lipoide in der medulla spinalis. Auch von anderer Seite wurden diese allgemeinen Befunde bestätigt (9, 12, 26). BERLINER (26) fand feine rote Granula in Leber, Milz und Lymphknoten, Hypophysenvorderlappen und Cornea. Auch er führte keine genaue Bestimmung durch, weist aber darauf hin, dass jene Granula sich von denen anderer Lipoidosen unterscheiden. ASHBY (2) fand vergrösserte Hypophyse und Schilddrüsenveränderungen. REILLY (46) sah grosse dunkelviolette Granula im Blut, Knochenmark und Milz, teils kleinere eosinophile. TUTHILL (39), der einen Fall Hurler's pathologisch untersuchte, fand hydrocephalus internus, Atrophie der Temporallappen, Lipoideinlagerungen in Ganglienzellen und myelin-freie Sehnerven, die von einem dichten Wall granulierter Zellen umgeben waren. Daneben fanden sich Tuberkel in Frontal- und Temporallappen.

Knochenschnitte liessen ein unregelmässiges Knorpelwachstum als Ursache der Wachstumshemmung erkennen. Doch ist wohl denkbar, dass daneben auch eine Störung der endesmalen Knochenbildung im Sinne unharmonischen Wachstums vorliegt. Das abnorme Wachstum der Schädelkalotte kann man als Folge eines hydrocephalus int. et ext. auffassen, womit jedoch nicht die Deformierung der excavatio hypophysea erklärt wird. Diese ist eine Folge der Entwicklungsstörung im primordialen Keilbein. Die Vergrösserung der endesmalen Schädelanteile ist aber nicht nur relativ, sondern absolut. Auch die Vergrösserung der clavicula über das Normale *hinaus* spricht hierfür.

Überraschend war das Ergebnis von LETTINGA (44), der einen Fall von DE LANGE (44) mikroskopisch untersuchte und eine Glykogenspeicherung als Ursache der Hepato-splenomegalie bei gleichzeitiger Cirrhose fand. Herz und Nieren waren glykogenfrei. Spuren von Phosphatiden in Nieren und Milz. Perisplenitis. Keine Gehirnlipoidose! Dieser Fall wurde von DE LANGE als »Typus E« bezeichnet, da er auch klinisch weder dem Hurler- noch dem Morquio-Syndrom angehörte. Der gleiche Fall wies auch eine tracheopathia chondroplastica, Otosklerose unterhalb der basalen Schneckenwindung, unvollkommene Pneumatisation beider Mastoidfortsätze, Knorpelfuge, Trommelfellverdickungen und Dehiszenzen in den Wänden des tympanum auf. Veränderungen, die für eine mangelhafte Ausbildung des primordialen Knochens sprechen.

Ophthalmologisch beschreibt WALSH (55) leichte Ptose, grosse dicke Lider und strabismus convergens. Normale Pupillarreaktion. Ev. Megalocornea mit folgendem Glaukom. Diffuse, langsam zunehmende, bilaterale, opake Trübung der Cornea durch Lipoideinlagerung im Stroma. Bowman'sche Membran und Epithel bleiben frei. Keine Vascularisation. Fundus ist gewöhnlich unsichtbar. Einzelne Fälle von Opticusatrophie, Papillenrötung und -Oedem.

Ätiologisch ist Heredität sichergestellt und liegt wahrscheinlich recessiver Erbgang vor. In mehreren Fällen (23, 26, 29, 32, 43) sind Angehörige einer Familie betroffen, z. T. Zwillinge, in anderen Fällen ist weder bei den Eltern noch in der Sippe ähnliche Erkrankung zu finden. Bei Entscheidung der Frage nach weiteren Geburten ist daher Vorsicht geboten. Wahrscheinlich besteht eine Keimschädigung. Die geistige Unterentwicklung, Corneatrübung, Hepato-splenomegalie und andere Veränderungen führt man auf eine Störung des Lipoidstoffwechsels zurück, die ihre bekannten Parallelen in den anderen Lipoidosen hat. Eine vorhergehende Infektion scheint als auslösende Ursache unwahrscheinlich. Die Pathogenese ist in ihren Einzelheiten noch unklar. Während einerseits behauptet wird, dass die Veränderungen bereits bei der Geburt vorliegen (25) ist in dem hier veröffentlichen Fall dies z. Teil sicher auszuschliessen. Kopf-Schulterumfang, Länge, Gewicht und äusseres Erscheinungsbild waren bei der Geburt normal.

Interessant sind in diesem Zusammenhang die Engel'schen Ansichten, der als Ursache der Chondrodystrophie eine Entwicklungsstörung der area membranacea anterior des 4. Ventrikels ansieht, durch die liquor cerebrospinalis austritt (sog. »blebs») und kleine herdförmige Reaktionen verursacht, die je nach ihrer Lage in der Nähe der Hypophyse und dem Hypothalamus zu Störungen im Lipoidstoffwechsel und Wachstum führen. Seine Theorie stützt sich hauptsächlich auf die Experimente von Bagg und Little und anderen Forschern (erwähnt in 25), die bei der Röntgenbestrahlung von Ovarien bei Mäusen Missbildungen an Extremitäten und Augen erzeugten und diese auf lokale Liquorreizung in der Subcutis der betroffenen Glieder zurückführten. In Parallele zu setzen ist hier die Theorie Staemmler's (51) für die Pathogenese der Syringomyelie. Er nimmt ebenfalls Defekte im Ependym des Zentralkanals an, durch die Liquor ins Parenchym austritt und eine Myelolyse und Gliawucherung hervorruft. Engel führt mit seiner Theorie die verschiedenen Wachstumshemmungen wie Hurler, Morquio, Oxycephalie, Acrocephalosyndactylie, pleonosteosis familiaris, ja sogar isolierte Missbildungen wie Klumpfuss auf *eine* Ursache zurück. Schwer erklärbar ist jedoch dabei die Heredität.

Der Streit, ob es sich um eine selbständige Lipoidose neben den bisher bekannten Formen Hand-Schüller-Christian, Letterer-Siwe, Eosinophiles Granulom, Gaucher, Niemann-Pick und Tay-Sachs (amaurotische Idiotie) handelt oder mit letzterer identisch ist oder aber überhaupt die ganze Gruppe eine gemeinsame Ursache hat, ist wohl nicht eher endgültig zu entscheiden bis durch verfeinerte biochemische Methoden die Gene e klargelegt werden kann oder doch, wie auch de Lange (43) sagt, die einzelnen Gruppen sicher differenziert werden können, wie dies z. B. bei der Glykogenspeicherkrankheit durch Mason und Anderson (47) geschah.

Eigener Fall: Der hier zu berichtende Fall ist eine klare Lipochondrodystrophie nach dem Hurlerschen Typus und betrifft einen 6 Jahre, 5 Monate alten Knaben, der im Westergrenschen Kinderkrankenhaus in Gävle vom 1. 6.—20. 7. 49 behandelt wurde. Krankengeschichte und Untersuchungsergebnisse wurden von dem leitenden und behandelnden Arzt (Dr. H. JELKE und Dr. A. L. BERGSTRÖM) freundlicherweise zur Verfügung gestellt und sollen stichwortartig wiedergegeben werden.

Heredität: Vater und Mutter gesund. Mutter bei Geburt 23 Jahre. Einziges Kind. Geburt normal. Gewicht: 2,980 gr. Länge 52 cm, Kopfumfang 33, Schulterumfang 35 cm. Cheilo-palatochisis! Allaitement mixte. Mit 2 Monaten Umbilicalhernie. Deutlich verlangsamte Entwicklung: 1. Zahn mit 14 Monaten, lernte gehen mit 20 Monaten. Sprach mit 13 Monaten einzelne Worte, Meinungen mit 3 Jahren. Cheilo-palatochisis zweizeitig operiert. 1948 Parotitis. Die Kyphose bemerkte die Mutter mit 9 Monaten als das Kind zu sitzen begann. Erhielt Gipsbett bis zum 2. Lebensjahr. Vom 2.—4. Jahre bemerkte die Mutter ein schnelles Anwachsen des Kopfes. Seitdem unverändert. Seit dem 3. Jahr kein Längenwachstum. Spricht alles, Konsonanten (st, sk, sp) schwer, versteht alles. Fast immer Rhinitis, kein Husten. Leicht Durchfälle.

Status: Altes Aussehen, grosser Kopf, deutlicher Gibbus über L_{1+2}. Klumpige Gesichtszüge, eingedellter Nasenrücken, Narbe nach Lippen- und Gaumenplastik, grosse fleischige Zunge. Heisere Stimme. Matte Corneae, schlaffe Haut, keine Zyanose, keine Oedeme. Unregelmässige, schlecht ausgebildete, spitze Zähne, 10/10. Keine Karies. *Herz:* Kurzes systolisches Geräusch über der Basis. P_2 acc., kein fremissement oder voussure. Extrasystolen. Spitzenstoss 6 cm von der linken Sternalkante. *Lunge:* o. B. *Abdomen:* Leber 3 Querfinger unter dem re. Rippenbogen, Milz 1 Querfinger unter dem li. tastbar. Bauchumfang 56.5. Starke Rektusdiastase, hühnereigrosse Umbilical-Rezidiv-Hernie mit Op.-Narbe. Testes descendiert. Länge 93.5 cm, Kopfumfang 55.5 cm, Brustumfang 56, Gewicht 17.1 kg. Dicke, kurze Extremitäten, Trommelschlegelfinger, in leichter Flexion semifixiert, auch passiv nicht streckbar. Faustschluss unmöglich. Endphalangen weichen radial ab.

Die Diagnose wurde klinisch gestellt. Die übrigen Untersuchungsbefunde weisen ausser einem relativen Hochdruck von 140/70 und einer deutlichen Vermehrung der Gesamtlipoide und des Cholesterins keine Besonderheiten auf. Blutbild: Segmentk. 30, Stabk. 6, Lymphz. grosse 10, kleine 46, Eos. 2, Mono 6, Erythr. 4.78 Mill. Hgb. 88 % = 13.5 g%. Skg. 15/45. Wa.R. neg. Kahn, Müllers Ballungsreaktion und Meinickes Klärungsreaktion neg. Plasmalipoide: Total 958 mg%. Cholesterin 255 mg%. Toxiplasmosereaktion neg. Glykosebelastung normal. Urin: Eiweiss neg., Zucker neg., Sed. neg., sauer. Faeces: Nichts patologisches. EKG. Rechtstyp, sonst normal.

Intelligenstest nach Terman-Merill: Intelligensquote 63, entsprechend einem Intelligensalter von 3 Jahren 11 Monaten. Psyche normal.

Abb. 1. 6 Jahre, 5 Monate alter Knabe mit Lipochondrodystrophie. Beachte den grossen Kopf, kurzen Nacken. Sattelnase, vorgetriebener Bauch, Umbilicalhernie, leichte Flexionstellung der Arme, Finger und Beine. Kyphose.

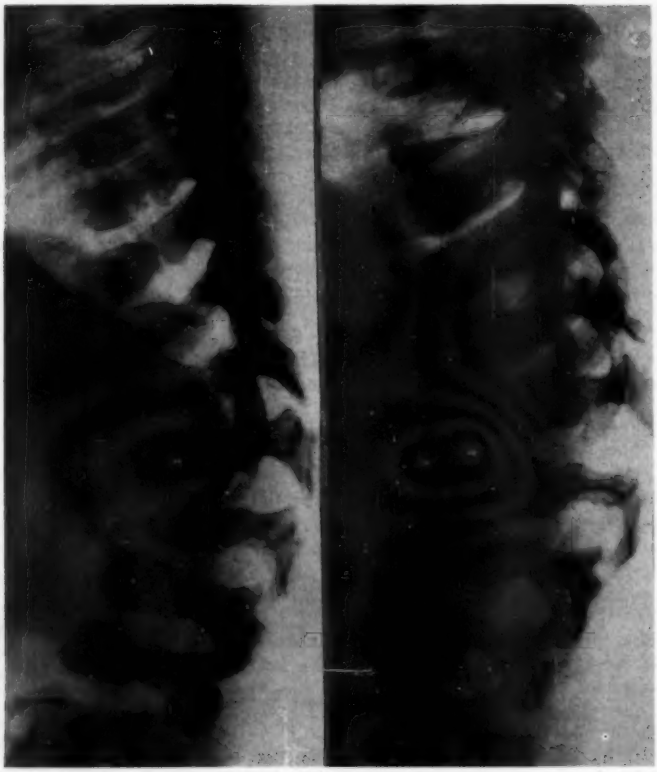


Abb. 2. Abb. 3.

Abb. 2. Aufnahme vom 22. 1. 44. (Pat. ist hier 10 Monate alt.) Typische Kyphose bei L_{1+2} mit hakenförmiger Deformierung der Wirbel.

Abb. 3. Das gleiche Bild am 19. 7. 1949. (Abb. 4—8 vom gleichen Tage.) Verstärkte Kyphose und Deformierung der benachbarten Wirbel. Zwischenwirbelscheiben intakt!

Augenstatus (Dr. TÖRNQUIST): »Sehschärfe wegen unzureichender Intelligens nicht prüfbar, Lider dick, keine Ptose. Bulbusstellung und Beweglichkeit o. B. Die Corneae sind beiderseits in der ganzen Ausdehnung diffus getrübt. Bei mikroskopischer Untersuchung sieht man eine kleinsprenklige Einlagerung im Cornealparenchym, die unmittelbar unter der Bowmanschen Membran beginnt und sich bis zur Hinterfläche der Cornea erstreckt. Die Membran selbst und das Epithel scheinen unbeschädigt. Cornea normalgross. Pupillen rund, gleichgross, reagieren prompt auf Licht und Convergens. Fundus schimmert nur schwach durch die getrübte Cornea hindurch, Einzelheiten sind nicht zu erkennen. Druck: palpatorisch normal. Die Corneaveränderungen stimmen vollkommen überein

Abb. 4. Humerus mit 115° Winkelstellung und mangelhafter Epiphysenbildung.

mit den bei Hurler's Syndrom beschriebenen.» Ausserdem fand sich ein kleines bedeutungsloses Adenoid. Laryngoskopie wurde nicht ausgeführt.

Nach BROMAN-DAHLBERG-LICHTENSTEIN (40) ist bei einer Länge von 93.3 cm, ein deutliches Zurückbleiben hinter der Norm festzustellen. Bei einem Alter von 6 Jahren, 5 Monaten sollte die Länge 117.0 cm $\pm$ 14.7 cm betragen. Im Gewicht ist die Diff. nicht so ausgeprägt. Norm: 21.2 kg $\pm$ 7.8 kg gegenüber 17.1 kg.

Röntgenologisch sind die meisten in der Literatur geschilderten Besonderheiten vorhanden. Um eine Wiederholung zu vermeiden, soll hier nur das vom bisherigen abweichende erwähnt werden.

Die ersten Röntgenbilder waren im Alter von 10 Monaten angefertigt, und das Kind wurde in der Folgezeit mehrfach geröntgt. Die Entwicklung des Skelettes konnte so verfolgt werden. Die ersten Bilder weisen in Höhe von L_{1+2} eine Kyphose von 35° auf mit den oben geschilderten Besonderheiten. In den folgenden 5 Jahren hat sich diese auf 60° verstärkt. L_1 ist am stärksten betroffen. Die 1944 deutlich sichtbaren Hahnschen Gefässkanäle und Knochendefekte an Stelle der unverkalkten Wirbelbogenepiphysen sind nun weniger gut sichtbar. Wenn auch die Kyphose auf L_{1+2} beschränkt ist, sind die benachbarten Wirbel doch ebenfalls abnorm geformt. Th_{10-12} u. L_{3-5} haben Keilform mit einer ventral cirka ½ höheren Kante als dorsal. Bei den Lendenwirbeln ist die kaudale Partie deutlich grösser. Diese Veränderungen sind um so ausgeprägter je näher die Wirbel der Kyphose liegen und haben sich in den letzten

Abb. 5. Unterarm und Hand. Beachte Form und Epiphysen von ulna und radius, Anzahl der Handwurzelknochen, Form und Struktur der Mittelhand und Finger.

Jahren verstärkt, wahrscheinlich infolge der anormalen Statik. Proc. transversi und spinosi sind in der unteren Brust- und Lendenwirbelsäule nur mangelhaft ausgebildet. Im Bereich der Kyphose scheinen die Gelenkfortsätze kaum noch Kontakt zu haben. Die Rippen sind riemenförmig, breit und reichen mit ihren plumpen tuberculi kaum an die proc. transversi heran. Collum und capitulum sind im Verhältnis zur Rippenbreite sehr schmächtig und beinahe rudimentär, was entweder auf einer

Abb. 6.

Abb. 7.

Abb. 6. Hüftgelenk mit flacher Pfanne. Coxa valga, gedoppelte Caputepiphyse, fehlende Trochanterepiphysen, klaffende Beckenepiphysen.

Abb. 7. Fuss mit den gleichen Entwicklungsstörungen wie an der Hand.

mangelhaften Verkalkung des osteoiden, röntgenstrahlendurchlässigen Gewebes beruht, oder einer tatsächlichen Verkürzung entspricht. Das zu entscheiden ist röntgenologisch nicht möglich. Auffallend ist, dass diese Verjüngung des Collum-Capitulum-Abschnittes in den letzten Jahren zugenommen hat und die Rippenenden mit 1-jährigem Alter normal aussehen. Während 1944 offene Wirbelbögen an C_7, $Th_{1,2,3,4,7}$, L_5, $S_{1,3,4,5}$ bestanden, sind diese jetzt nur noch an der unteren Lenden- und Sacralwirbelsäule sichtbar. Die anfangs weit klaffenden Beckenepiphysen haben sich nur wenig genähert und stehen weit hinter der normalen Entwicklung zurück. Die Hüftgelenke haben unverändert weite und flache Pfannen. Die Epiphysen der Femurköpfe sind rudimentär und haben sich seit 1944 nur wenig vergrössert, die rechte ist gedoppelt. Es fehlen die Epiphysenkerne für: multangulum majus, minus, naviculare, distale Ulnaepiphyse, proximale Epiphyse dig. I, Epiphysen der Endphalangen 1, 2 u. 5, naviculare pedis, distale Metatarsalepiphysen 2—5, Mittelpha-

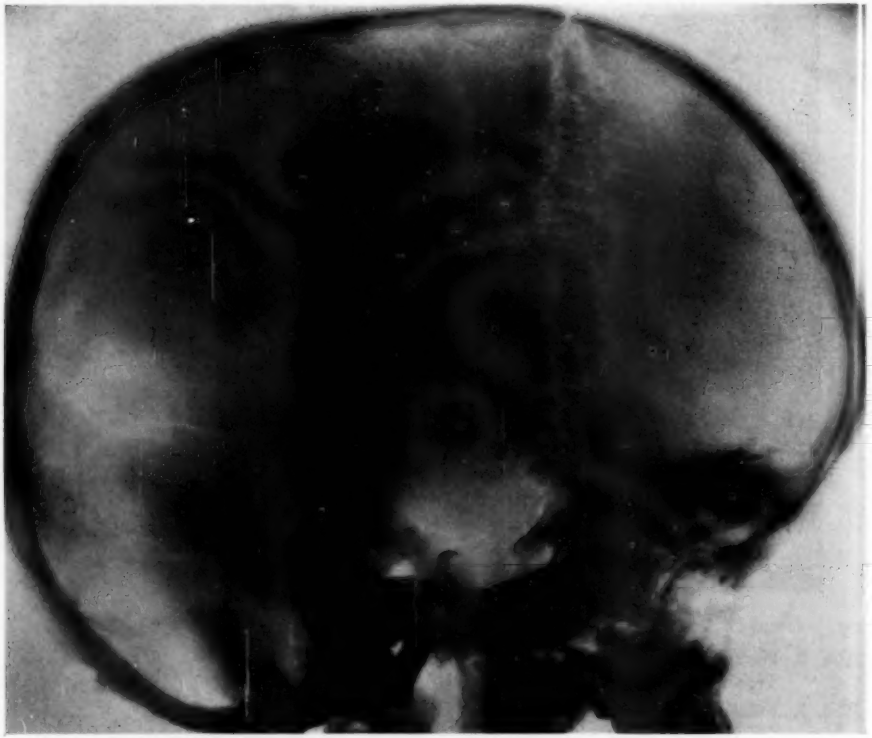


Abb. 8. Schädel. Scaphocephalus, wahrscheinlich hydrocephalus int. et ext., dünne Kalotte, deutliche Gefässzeichnung, klaffende Suturen, lange flache excavatio hypophysea, mangelhafte Pneumatisation.

langen 3—5, Endphalangen 2—5, proximale Fibulaepiphyse, patella, trochanter major und minor. Eine genaue Zählung der Epiphysenkerne nach ELGENMARK (41) ergab 44 Kerne, was bei einer Variationsbreite von $\pm$ 4.8 einem Alter von 31—33 Monaten entspricht. Das Herz misst in der Länge 11.5 cm, Breite 9.0 cm und in sagittaler Richtung 8 cm. Das absolute Volumen nach DU BOIS (54) beträgt 345 ccm, entsprechend einem relativen Volumen von 215 ccm per qm Körperfläche.

Bereits auf den ersten Filmen ist im Alter von 10 Monaten eine leichte Vergrösserung der Leber zu sehen, die im Laufe der Jahre bedeutend zugenommen hat. Sie reicht jetzt bis zur crista iliaca. Auch die Milz ist deutlich vergrössert.

Behandlung und Prognose

Die Behandlung besteht lediglich in konservativen, orthopädischen Massnahmen, die die Zunahme der Kyphose verhindern sollen. Hormonale Therapie war bisher nutzlos. Eine Erkrankung der Nieren liegt nicht vor. Die Prognose ist schlecht. Der Tod erfolgt meist an einer interkurrenten Herz- oder Lungenerkrankung vor dem 20. Lebensjahre.

Differentialdiagnostisch sind auszuschalten:

1. Morquio's Syndrom, das ohne Schädelveränderungen, geistige Entwicklungsstörungen, Hepatosplenomegalie und Corneatrübungen einhergeht. Nach CRAWFORD (24) und ELLIS (14) soll auch die Kyphose mehr graduelle Unterschiede aufweisen. Statt coxa valga findet sich coxa vara. Schlappe, nicht fixierte Gelenke. Die bei HARVEY (25) angegebenen Unterscheidungsmerkmale, dass bei Hurler's Syndrom nur 2 Wirbel verändert seien und alle Veränderungen seit der Geburt beständen, kann ich nicht bestätigen.

2. Achondroplasia. Nach RUGGLES (7) schliessen sich hier die Epiphysen verfrüht. Der Körper erscheint lang im Verhältnis zu den Extremitäten.

3. Hypothyreoidismus (Kretin), weist ebenfalls verzögerte Epiphysenbildung auf, unterscheidet sich aber durch die fehlenden Kardinalsymptome.

Ebenfalls lassen sich rein röntgenologisch die folgenden Krankheitsbilder trennen: Chronische Polyarthritis, traumatische Wirbelverletzungen, Wirbeltuberkulose, Pott's Krankheit, Ollier's Krankheit, hypophysäre Zwerge, Chondrodystrophia foetalis, Scheuermann, Rachitis tarda, Dysostosis cranio-facialis, -cleido-cranialis, Arachnodactylie und die oben erwähnten Lipoidosen.

ZUSAMMENFASSUNG

Beschrieben wird ein 6 Jahre, 5 Monate alter Junge, der alle typischen klinischen und röntgenologischen Zeichen einer Lipochondrodystrophie (Hurler's Syndrom) aufweist. Die einschlägige Literatur wird besprochen.

SUMMARY

A typical case of lipochondrodystrophy (Hurler's Syndrome) is reported in a boy of 6 years and 5 months, showing all the clinical and roentgenological symptoms. The literature is discussed.

RÉSUMÉ

Description du cas d'un garçon de 6 ans et 5 mois présentant de façon typique tous les signes cliniques et rœntgenologiques d'une lipochondrodystrophie (Syndrome de Hurler). La littérature se rapportant à cette affection fait l'objet de considérations.

SCHRIFTTUM

1. Hurler, G., Über einen Typ multipler Abartungen, vorwiegend am Skelettsystem. Zeitschrift für Kinderheilkunde 1919, 24, 220.
2. Pfaundler, M., Demonstrationen über einen Typus kindlicher Dysostose. Jahrb. för Kinderheilkunde 1920, 92, 420.
3. Morquio, Sur une forme de dystrophie osseuse familiale. Arch. de méd. d. enf. 1929, 32, 129.
4. Brailsford, J. F., The Radiology of bones and joints. William Wood and Co., Baltimore 1935.
5. Putnam, M. C. und Pelkan, K. F., Case of scaphocephaly with malformations of the skeleton and other tissues. Am. J. Dis. Child. 1925, 29, 51.
6. Meyer, H. F. und Brennemann, J., A rare osseous dystrophy (Morquio). A. J. Dis. Child. 1932, 43, 123.
7. Ruggles, H. E., Dwarfism due to disordered epiphyseal development. A. J. Roent. and Rad. Therapy 1931, 25, 91.
8. Reilly, W. A., Dysostosis multiplex. Endocrinology 1938, 22, 616.
9. Aegerter, E. E. und Kressler, R. J., Hurler's syndrome (gargoylism). J. Pediatr. 1938, 12, 579.
10. John Caffey, Pediatric X-Ray diagnosis. The Year Book Publishers. Inc. 1945, 49.
11. Hubeny, M. J. und Delano, P. J., Dysostosis multiplex. Am. J. Roentg. 1941, 46, 336.
12. Ashby, W. R., Steward, R. M. und Watkin, J. H., Chondro-osteo-dystrophy of the Hurler type (gargoylism). Pathological study. Brain, 1937, 60, 149.
13. Brown, D. O. und Macdonald, C., Three cases of familial osseous dystrophy. Australia und New Zealand J. Surg. 1933, 3, 78—88.
14. Ellis, R. W. B., Sheldon, W. und Capon, N. B., Gargoylism. Quart. J. Med. 1936, 5, 119.
15. Ellis, R. W. B., Hepatosplenomegaly with mental deficiency and bone changes. Proc. Roy. Soc. Med. 1934, 27, 1022.
16. —, Gargoylism. Proc. Roy. Soc. Med. 1936, 30, 158.
17. —, Gargoylism. Proc. Roy. Soc. Med. 1938, 31, 770.
18. Golding, F. C., Chondro-osteo-dystrophy. Brit. J. Radiol. 1935, 8, 457.
19. Hirsch, J. S., Generalized osteochondrodystrophy, eccentrochondroplastic form. J. Bone and Joint Surg. 1937, 19, 297.
20. Russo, P., Chondro-osteo-dystrophy. Morquio's disease. Radiology, 1943, 41, 42.
21. Larson, Sidney und Lichty, John A. jr., Gargoylism. A. J. of Roentg. 1943, 50, 61.
22. Washington, J. A., Lipochondrodystrophy. Chap. XXX in: Pratice of Pediatrics Vol. IV, edited by Joseph Brennemann. W. F. Prior Co. Hagerstown, Maryland 1937.

23. ENGEL, D., Etiology of multiple deformities. A. J. Dis. Child. 1940, 60, 562.
24. CRAWFORD, T., Case of Morquio's disease. Arch. Dis. Childhood 1939, 14, 70.
25. HARVEY, R. M., Hurler-Pfaundler Syndrome (Gargoylism). A. J. of Roentg. 1942, 48, 732.
26. BERLINER, M. L., Lipin keratitis of Hurlers syndrome (gargoylism or dysostosis multiplex). Arch. Ophth. 1939, 22, 97.
27. BESDZIEK, J., Zur Kenntnis der angeborenen Missbildungen des Skeletts. Monatsschrift der Kinderheilkunde 1938, 76, 305.
28. BINDSWANGER, E. und ULLRICH, O., Über die Dysostosis multiplex (Typus Hurler) und ihre Beziehungen zu anderen Konstitutionsanomalien.
29. BINDSCHEDLER, J. J., Polydystrophie du type Hurler chez un frère et une soeur. Bull. Soc. péd. de Paris, 1938, 36, 571.
30. TEN BOKKEL HUININK, A., Gargoylism (Chondro-osteo-dystrophy, corneal opacity, hepatosplenomegaly and mental deficiency). Maandschr. v. kindergeneesk. 1937, 6, 449.
31. COCKAYNE, E. A., Hepatosplenomegaly associated with mental deficiency and bone changes. Proc. Roy. Soc. Med. 1935, 28, 1067.
32. —, Gargoylism (Chondro-osteo-dystrophy, hepatosplenomegaly, deafness) in two brothers. Proc. Roy. Soc. Med. 1936, 30, 104.
33. LIEBENHAM, L., Beitrag zur Dysostosis multiplex. Zeitschrift für Kinderheilkunde 1937, 59, 91.
34. MEYER, S. J. und OKNER, H. B., Dysostosis multiplex with special reference to ocular findings. Am. J. Ophth. 1939, 22, 713.
35. NORDMANN, J., Deux cas de gargoylisme. Bull. soc. d'ophth. Paris, 1937, 49, 256.
36. POYNTON, F. J., LIGHTWOOD, R. und ELLIS, R. W. B., Hepatosplenomegaly with mental deficiency and bone changes. Proc. Roy. Soc. Med. 1934, 27, 1025.
37. SHELDON, W., Form of gigantism with splanchnomegaly. Proc. Roy. Soc. Med. 1934, 27, 1003.
38. SLOT, G. und BURGESS, G. L., Gargoylism. Proc. Roy. Soc. Med. 1938, 31, 1113.
39. TUTHILL, C. R., Juvenile amaurotic idiocy. Arch. Neur. and Psych. 1934, 32 198.
40. BROMAN B., DAHLBERG, G. und LICHTENSTEIN, A., Height and weight during growth. Acta Pediatr. XXX, 1942, 1.
41. ELGENMARK, O., The normal development of the ossific centres during infancy and childhood. Acta Paediatr. 1946. Suppl. I.
42. MITCHELL-NELSON, Textbook of Pediatrics. 4th edition. Saunders Company, Philadelphia and London 1947, 1189.
43. DE LANGE, C., GERLINGS, P. G., KLEYN, A. und LETTINGA, T. W., Some remarks on gargoylism. Acta Paediat. 1944, XXX, 398.
44. DE LANGE, C. Über dysostosis multiplex, Typus Hurler und Gargoylism. Psych. Bl. 1942, 46, 2.
45. SCHMIDT, M. B., Die anatomischen Veränderungen des Skeletts bei der Hurlerschen Krankheit. Zbl. Path. 1942, 79, 113.
46. REILLY, W. A., The granules in the leukocytes in gargoylism. A. J. Dis. Child. 1941, 62, 489.
47. MASON, H. H. und ANDERSSON, D. H., A. H. D. Ch. 1941, 63, 765.
48. KNY, W., Zeitschrift für Kinderheilkunde 1942, 63, 366.
49. DE RUDDER, B., Zeitschrift f. Kinderheilkunde 1942, 63, 407.
50. JEWESBURY, R. C. und SPENCE, J. C., Oxycephaly, Proc. Roy. Soc. Med. 1920/21, 14, 27.
—, Acrocephaly with other congenital deformities. Proc. Roy. Soc. Med. 1920/21, 14, 30.

51. Staemmler, erwähnt in Ribbert-Hamperl, Lehrbuch der allgemeinen Pathologie und der pathologischen Anatomie, Springer Verl. Berlin, 1944, 17. Aufl., 391.
52. Henderson, J. S., Gargoylism, review of principal features with reports of 5 cases. Arch. Dis. Childhood 1940, 15, 201.
53. Simons, B., Röntgendiagnostik der Wirbelsäule, Fischer Verlag, Jena 1939.
54. du Bois et du Bois, Arch. Int. Med. 1915, 15, 858; 1916, 17, 865.
55. Walsh, F. B., Clinical Neuro-ophthalmology. The Williams and Wilkins Comp. Baltimore 1947, S. 471.

FROM THE I. ROENTGENDIAGNOSTIC DEPARTMENT OF SÖDERSJUKHUSET, STOCKHOLM, SWEDEN (HEAD: DOCENT G. JÖNSSON)

IMPRESSION FRACTURES IN THE CAPUT HUMERI IN CONNECTION WITH ELECTROSHOCK[1]

by

Tore Sylwan

The risk of fractures arising in connection with shock treatment for mental disease is not inconsiderable. Spasms of both the tonic and the clonic type, resembling those seen in connection with epileptic attacks, occur during the treatments. In all probability, the trauma that causes the fractures consists to a large extent in the body's own muscular contractions. This is particularly the case with the compression fractures in the upper and middle segments of the thoracic part of the vertebral column, the type of fracture which is by far the most commonly observed. Statements in the literature regarding the incidence of fractures of the vertebrae show much variation, ranging from 0.5 to 43 per cent. FLORDH has reported from the South Stockholm Hospital (Södersjukhuset) that he found these fractures in 9 per cent of all patients submitted to electroshock treatment.

Fractures of the humerus, on the other hand, are rare occurrences in connection with shock treatment, according to what can be ascertained from the literature. COOK, after studying several different groups of patients treated by various forms of shock, stated the frequency of fractures of the humerus to be 0.24 per cent. For the rest, these fractures have been reported in only a few isolated cases; in most of these cases the damage was severe, with considerable dislocation. During 1948, we encountered at the South Stockholm Hospital five cases of compression fracture in the caput humeri after electroshock of a type not previously described in this connection. In all of these patients the injury took the form of an impression in the medial part of the head, close to the tuberculum minus (see illustrations). In one patient (fig. 2 c) there was also a fissure through the base of this tubercle.

[1] Submitted for publication Aug. 29, 1949.

Fig. 1 a. Fig. 1 b.

Fig. 1 a—b. Case 1. Impression fracture in the medial part of the caput humeri, 1 cm deep, close to the medial rim of the lesser tubercle.

Clinical Data Concerning the Cases

The shock treatment had been given in accordance with the customary method, with the patient in the supine position on a hard bench with a small firm cushion under the thoracic kyphosis. One assistant held the hips and another the shoulders against the underlying support. The signs of injury to the skeleton appeared when the patient returned to consciousness after the shock treatment, and in three cases they were very mild. In two cases there were distinct clinical signs of skeletal damage. In one of these patients, dislocation of the shoulder joint, in a backward direction, judging from the outward appearances, occurred on several occasions — without any apparent force being applied — during the days immediately following the injury. There was no time to verify the dislocation by roentgenology as spontaneous reduction occurred each time.

The last-mentioned case is interesting because it gives some indication of the probable mode of origin of these impression fractures. There is, in point of fact, strong reason to believe that the fractures arise as the result of a temporary dorsal dislocation of the shoulder during the spasms caused by the shock, in connection with which the medial portion of the caput humeri is pressed against the posterior edge of the glenoid cavity.

Fig. 2 a.

Fig. 2 b.

Fig. 2 c.

Fig. 2 a—c. Case 4. Impression of the medial part of the caput humeri. In one axial view (fig. 2 c), a fissure is distinguishable through the base of the lesser tubercle.

Fractures at the site in question — in some cases in conjunction with fractures through the diaphysis of the humerus or the tuberculum minus — are mentioned both in shorter publications and in textbooks of surgery and roentgenology as being a complication of dorsal dislocation of the shoulder. I have not found any mention of such fractures in other connections, or as an isolated phenomenon.

The extremely rare dorsal dislocations of the shoulder-joint are stated to occur chiefly in connection with epileptic attacks, which bear a close resemblance to the spasms occurring during shock treatment. Insulin coma also produces spasms of this kind. Figs. 4 and 5 show the shoulders of a 38-year-old diabetic who was treated at the First Surgical Clinic of the South Stockholm Hospital in November 1948. This patient developed typical impression fractures on the medial aspect of the caput humeri, on both sides, during insulin coma. In the right shoulder there also developed a permanent backward dislocation as well as a fracture through the tuberculum minus (fig. 4). The picture shows clearly how the posterior glenoid rim has been pressed into the caput humeri.

Fig. 3 a. Fig. 3 b.

Fig. 3 a—b. Case 5. Impression of the caput, medial to the lesser tubercle. In fig. 3 a, as in fig. 2 a, the fracture can be seen in the usual antero-posterior view (between arrows).

Dorsal dislocation of the shoulder-joint arises as the result of strong inward rotation and adduction of the humerus straight across the chest, with force, either direct or indirect, applied simultaneously on the caput. This position of the humerus is common, and often extreme, during the spasms produced by electroshock. While in the supine position the patients usually make a violent effort to raise the upper part of the body from the underlying support. When their shoulders are pressed in a dorsal direction by the assistant while at the same time the remaining parts of their arms are allowed freedom of movement the conditions for the production of a dislocation are thus fulfilled.

Even on an ordinary antero-posterior radiogram of the head of the humerus in a position of inward rotation the fracture is seen as a thin marginal area separated from the substantia spongiosa by an even rim of increased density (fig. 3 a). This rim can readily be mistaken for the proximal demarcation line of the tuberculum minus, and this type of fracture is easily overlooked if the possibility of its presence is not borne in mind. If the impression is shallow, views must be taken with the ray at a tangent to the part of the caput humeri under examination. Because of the individual differences in the posture of the shoulder girdle, such an examination is often rather time-consuming. KNUTSSON has recently worked out a standard adjustment for axial views of the shoulder-joint. This was not used in the cases mentioned in the present communication, but it would seem to be a valuable method to apply when this type of fracture is suspected.

Fig. 4. Fig. 5.

Fig. 4. Patient not treated for mental disease. Backward dislocation of the right shoulder-joint, established after an accidental insulin coma. The head of the humerus is pressed against the dorsal edge of the glenoid cavity, causing a very deep impression fracture in the medial part of the head.

Fig. 5. The same case as in fig. 4. Left shoulder. There is no dislocation of the joint but an impression fracture of the same type as in figs. 1—4 is visualized.

The five cases were encountered during a six-month period. The number of patients given electroshock treatment at this hospital during the whole of 1948 was 150. This complication of electroshock is possibly not uncommon at other hospitals also. One of the reasons why it has not previously been described may be that the clinical signs and symptoms are not at all pronounced, and many patients with shoulder injuries consequently fail to be referred to the Roentgen Department for examination.

SUMMARY

A complication of electroshock treatment for mental disease, in the form of an impression fracture in the caput humeri medial to the lesser tubercle, has been observed in five cases. The fractures arose without doubt as the result of temporary dorsal luxation of the shoulder-joint during the spasms. They are readily overlooked at the roentgen examination if the possibility of their presence is not borne in mind.

ZUSAMMENFASSUNG

Als Komplikation zur Behandlung von psychisch Kranken mit dem Elektroschock kamen 5 Fälle von Impressionsfraktur des Caput humeri medial vom Tuberculum minus zur Beobachtung. Die Frakturen sind sicher durch kurzdauernde Dorsalluxation im Schultergelenk entstanden. Sie werden bei der Röntgenuntersuchung leicht übersehen, wenn man nicht im Voraus darauf eingestellt ist, dass sie vorkommen können.

RÉSUMÉ

L'auteur a observé cinq cas de fracture de la tête humérale, par tassement, au-dessus du trochin, venant compliquer le traitement d'aliénés par l'électrochoc. Ces fractures sont certainement survenues par une luxation dorsale passagère de l'articulation scapulo-humérale. Elles passent facilement inaperçues lors de l'examen radiologique si l'on n'est pas d'avance alerté quant à leur possibilité.

REFERENCES

Cook, L. C.: J. Ment. Sci. *378*: 435. 1944.
Flordh, P.: Nord. Psyk. Föreningsblad *3*: 169. 1949.
Hermodsson, I.: Acta Radiol. Suppl. 20. 1934.
Kalinowsky, L. B. & Hoch, P. H.: Shock Treatments and other somatic procedures in Psychiatry. New York 1946.
Knutsson, F.: Acta Radiol. *30*: 214. 1948.
Moseley, H. F.: Shoulder Lesions. Montreal 1945.
Rendich, R. A. & Poppel, M. H.: Radiology *36*: 42. 1941.
Schinz, H. R., Baensch, W. & Friedl, E.: Lehrbuch der Röntgendiagnostik. Leipzig 1939.
Watson-Jones, R.: Fractures and Joint Injuries. Edinburgh 1939.

FROM THE ROENTGEN DEPARTMENT OF THE SERAFIMER HOSPITAL, STOCKHOLM, SWEDEN
(CHIEF: PROFESSOR ERIK LINDGREN)

PRESSURE CHANGES IN THE SELLA TURCICA IN THE PRESENCE OF GLIOMA IN THE CEREBRAL HEMISPHERES[1]

by

Bengt Nordmark

In SCHITTENHELM's »Lehrbuch der Röntgendiagnostik» published in 1924, SCHÜLLER writes in his rightly famous section »Röntgendiagnostik der Erkrankungen des Kopfes»: »Bei chronischer Hirndrucksteigerung macht sich als Teilerscheinung der allgemeinen Usur der Schädelinnenfläche in sehr auffälliger Weise auf dem Profilbilde des Schädels die Destruktion der Knochenvorsprünge am Eingang der Sella turcica bemerkbar. Die Form der Destruktion entspricht vollkommen derjenigen, welche durch basale Hirngeschwülste erzeugt ist (Verdünnung und Vertiefung des Bodens der Sella, Verdünnung und Verkürzung der Sattellehne, Zuschärfung der Processus clinoidei ant.).» As the cause of increased intracranial pressure, SCHÜLLER mentions chronic hydrocephalus and brain tumours with varying localisations.

Many authors after SCHÜLLER consider, however, that the only cause of pressure changes in the sella turcica is an enlargement of the 3rd ventricle. This enlarged 3rd ventricle affects the sella turcica in part through a continual pressure and in part through constant pulsation and in that way causes decalcification and erosion of the bony processes at the entrance to the sella turcica, dorsum sellae and the sella bottom. STENVERS also writes: »Ist bei hohem intrakraniellem Druck eine Erweiterung des dritten Ventrikels unmöglich, so entsteht keine sekundäre Erweiterung der Sella turcica.»

This contention has later been contradicted by several authors, especially LÜDIN, KORNBLUM and OSMUND. In a work from 1935 the latter two discuss different factors also, which contribute to the origin

[1] Read at the Meeting of the Northern Association for Medical Radiology, Stockholm, June 10—12, 1949; submitted for publication, July 30, 1949.

of pressure sella, as for example the species of the tumour, the rate of growth and its site.

There are accordingly, two types of pressure sella, the one caused by a hydrocephally dilated 3rd ventricle and the other caused by an expanding intracranial process without hydrocephalus. The changes with the first type correspond to those which are caused by a suprasellar tumour. The changes with the second type I shall describe later in detail.

If and to what extent pressure changes in the sella turcica occur in the case of different gliomas is disputed. In order to throw some light upon this question I have studied a series of glicmas in the cerebral hemispheres from the 4 year period 1944—1947. Only gliomas in the cerebral hemispheres are included in order to preclude the possibility of pressure changes having originated over a dilated 3rd ventricle. Tumours in the cerebral hemispheres may also, in rare cases, it is true, be so situated that they give rise to a hydrocephalus. However, no cases of this sort are included in the material.

The sellar changes in this material have been classified in three groups: small, medium and large changes.

The first demonstrable change in the sella turcica when there is increased intracranial pressure is a thinning of the corticalis, which in the beginning is most clearly noticeable in the anterior wall contour of the dorsum and at times in the sella bottom. The pictures in fig. 1 are from the same patient, one about a week before and the other two years after the operation of an astrocytoma in the left frontal lobe. The thinning of the corticalis in the anterior wall contour of the dorsum and in the most posterior part of the sella bottom seen before the operation has completely receded at the time of the later examination.

In old people osteoporosis of the entire skeleton often ensues, which, of course, is observed in the sella turcica as well. This senile atrophy appears, however, in the entire sella turcica and the skull moreover, and not as an isolated thinning of the corticalis in the dorsum and the bottom of the sella turcica, as is the case with early symptoms of intracranial pressure. (See fig. 2.)

In the group with small pressure changes the sellar contours are still well preserved. In the group with medium changes the corticalis has partially disappeared and in the dorsum and sella bottom there are obvious defects. (See fig. 3.)

The sphenoid sinus often extends back under the sella bottom and sometimes up in the dorsum. A sphenoid cavity so situated forms a considerably greater resistance to the increased intracranial pressure than spongy bone. This is certainly the reason why pressure changes in the sella turcica are, as a rule, first demonstrable in the dorsum and posterior part of the sella bottom.

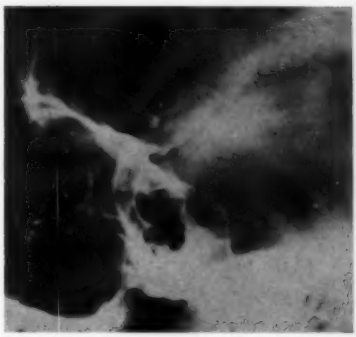


Fig. 1 a. Small pressure changes in the sella turcica.

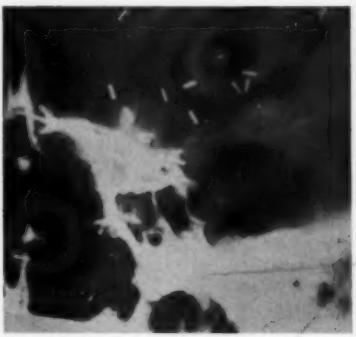


Fig. 1 b. The same case two years after the operation of an astrocytoma in the left frontal lobe.

Fig. 2 a. Senile atrophy.

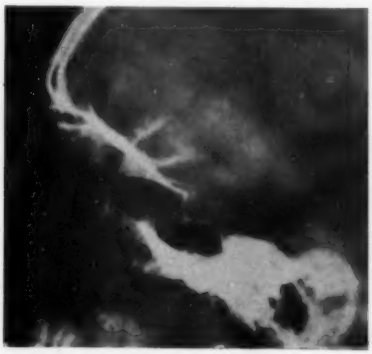


Fig. 2 b. Small pressure changes in the sella turcica.

Defects in the sellar contours also just before the sphenoid sinus are first encountered in the group with large pressure changes. (See fig. 4.)

I have found destruction within the area of tuberculum sellae or of the anterior clinoid process in only the cases in which the tumour was sited immediately beside these skeletal parts and could thus exercise a direct pressure upon them.

The material consists of 199 cases examined in the roentgen department and verified with pathologic anatomic diagnosis either at operation or post mortem. Cases with uncertain pathologic anatomic diagnosis have not been included in the material. The 199 verified cases

Fig. 3. Medium pressure changes in the sella turcica. The sphenoid cavity forms a greater resistance to the increased intracranial pressure than spongy bone.

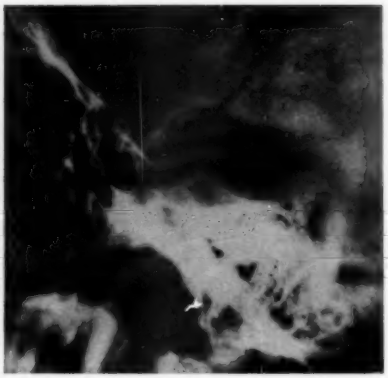


Fig. 4. Large pressure changes in the sella turcica. Defects in the sellar contours also just before the sphenoid cavity.

are made up of 119 malignant gliomas, almost 2/3 of the material. 64 are astrocytomas and 16 are oligodendrogliomas. Their distribution according to the localisation in different lobes is evident from the attached table. The most common localisation is, accordingly, in the frontal and temporal lobes. A smaller number are sited in the parietal lobes and only a few in the occipital lobes.

From the table it is evident that pressure sella occurs in 100 % of the cases with localisation in the occipital lobes. It is, however, a question of only 7 cases, therefore it is perhaps a coincidence, but in all events it appears to be worthy of note. Glioma in the other lobes has been accompanied by pressure changes in the sella turcica in approximately 50 % of the cases. With malignant glioma in the parietal lobe, however, changes occur in 70 %. Accordingly, no obvious differences, referring to the incidence of pressure sella with varying tumour localisation, were present in this material.

The occurrence of papillary stasis and pressure changes in the sella turcica is almost the same. However, papillary stasis is more common as a rule and in most cases is a somewhat earlier symptom of increased intracranial pressure than is pressure sella.

The symptom time — period of anamnesis — is noticeably shorter for the malignant gliomas than for the others. Where the symptom time may be counted in years in cases of astrocytoma and oligodendroglioma, with malignant glioma it is a matter of approximately the same number of months. The cases of malignant glioma without pressure changes

Table

	Nr	Symptom time		Papillary stasis		Pressure sella		Pressure changes:			
		with	without								
		sellar changes		Nr	%	Nr	%	No Nr	Small Nr	Medium Nr	Large Nr
Malignant gliomas.											
Frontal lobe	41	7 m.	3 m.	29	70	23	56	18	7	15	1
Tempor. lobe	45	11 m.	4 m.	31	69	22	49	23	13	8	1
Pariet. lobe	27	1 y. 1 m.	8 m.	16	59	19	70	8	4	14	1
Occipit. lobe	6	5 m.	—	3	50	6	100	—	1	5	—
Astrocytomas.											
Frontal lobe	30	3 y. 6 m.	3 y.	19	63	20	67	10	6	9	5
Tempor. lobe	22	2 y. 6 m.	4 y.	10	45	12	55	10	4	6	2
Pariet. lobe	11	5 m.	1 y. 6 m.	6	55	5	46	6	2	3	—
Occipit. lobe	1	1 y.	—	1	100	1	100	—	—	1	—
Oligodendrogliomas.											
Frontal lobe	10	2 y. 6 m.	5 y.	5	50	5	50	5	—	5	—
Tempor. lobe	4	9 m.	8 y.	1	25	1	25	3	—	1	—
Pariet. lobe	2	3 m.	2 y.	1	50	1	50	1	1	—	—
Occipit. lobe	—	—	—	—	—	—	—	—	—	—	—

y = years
m = months

in the sella turcica have throughout about half as long a symptom time as the cases with pressure changes in the sella. When the symptom time is one month or less, pressure changes in the sella turcica are very unusual. They do occur, nevertheless, but it is always only a matter of small sellar changes. In regard to astrocytoma and oligodendroglioma there is no relation in this material between the length of the symptom time and the occurrence of pressure sella. The cases with as well as those without pressure sella in the presence of benign glioma on the average have anamnesis periods counted in years.

Small as well as medium and large pressure changes in the sella turcica occur both with malignant glioma and with astrocytoma and also with oligodendroglioma. The incidence of small pressure changes in the sella turcica with malignant glioma is only slightly greater than with benign glioma.

In this material pressure changes in the sella turcica with malignant glioma occur in 58.8 % of the cases and with the benign gliomas taken all together, in 56.2 % . A comparison of the incidence with malignant and benign glioma, accordingly, shows no difference. Consequently, there is no possibility, through the incidence of pressure changes in the

sella turcica, of drawing any conclusions concerning the malignancy of the tumour which has been established with contrast examination of the ventricular system or vessels of the brain.

SUMMARY

Pressure changes in the sella turcica with glioma in the cerebral hemispheres without a hydrocephally dilated 3rd ventricle have been studied in a material consisting of 199 cases from a 4 year period 1944—1947. The first change consists of a thinning of the corticalis most clearly noticeable in the contour of the anterior wall of dorsum and at times in the sella bottom. Later the corticalis partially disappears and obvious defects appear in dorsum sellae and in the sella bottom. A sphenoid sinus situated under sella bottom forms a greater resistance against increased intracranial pressure than spongy bone. Defects in sellar contours also just beside the sphenoid sinus are first encountered with large pressure changes. No obvious variation in the incidence of pressure sella with different tumour localisation occurred in the material. With malignant glioma there are pressure changes in the sella turcica in 58.8 % of the cases and with the benign gliomas taken all together, in 56.2 %. Thus the occurrence of pressure sella does not justify any conclusions regarding the malignancy in an established tumour.

ZUSAMMENFASSUNG

Druckveränderungen im Türkensattel bei Gliomen der Grosshirnhemisphären ohne hydrozephal. erweiterten 3. Ventrikel wurden an einem Material von 199 Fällen aus den vier Jahren 1944—1947 studiert. Die erste Veränderung besteht in einem Dünnerwerden der Kortikalis, was am vorderen Wandumriss des Dorsum und manchmal am Boden der Sella am deutlichsten hervortritt. Später verschwindet die Kortikalis teilweise, und am Dorsum sellae sowie am Boden des Sattels treten deutliche Defekte hervor. Ein unter dem Boden des Sattels liegender Sinus sphenoidalis bietet einem gesteigerten intrakranialen Druck grösseren Widerstand als spongiöser Knochen. Erst bei starken Druckveränderungen findet man Defekte der Kontur des Sattels auch gegenüber dem Sinus sphenoidalis. Ein deutlicher Unterschied inbezug auf das Auftreten von Drucksella bei verschiedener Lokalisation von Tumoren war im Material nicht erkennbar. Bei malignen Gliomen kommen Druckveränderungen des Türkensattels in 58.8 % vor und bei gutartigen Gliomen im ganzen in 56.2 %. Das Vorliegen einer Drucksella berechtigt also nicht zu irgendwelchen Schlussfolgerungen über die Bösartigkeit eines nachgewiesenen Tumors.

RÉSUMÉ

Sur la base d'un matériel de 199 cas des 4 années 1944—1947 on a étudié les altérations de la selle turcique par hypertension dans les gliomes des hémispheres cérébraux non accompagnés de dilatation hydrocéphalique du 3e ventricule. La modification la plus précoce consiste en un amincissement de la corticale, qui s'observe le plus nettement sur les contours antérieurs du dos de la selle, et parfois au fond de cette dernière. Plus tard, la corticale disparait en partie et des lacunes bien visibles se montrent au dos et au fond de la selle. Un sinus sphénoïdal situé sous le plancher de la selle oppose à l'augmentation de la pression intracranienne une résistance plus forte que ne le ferait l'os spongieux. Ce n'est qu'en cas de graves changements dans la pression qu'on rencontre même juste en regard du sinus sphénoïdal des lacunes dans les contours de la selle. Dans ce matériel la diversité de localisation de la tumeur ne s'est pas traduite par des différen-

ces dans la fréquence d'apparition de l'image de compression de la selle. Dans les gliomes malins on trouve des altérations de la selle turcique par changement de pression dans 58.8 % des cas, et dans les gliomes bénins, tous ensemble le chiffre est de 56.2 %. La présence de signes de compression au niveau de la selle n'autorise donc pas à tirer de conclusions quant à la malignité d'une tumeur dont l'existence a été constatée.

REFERENCES

Bokelmann, O.: Die spec. Anatomie der Sella turc. und ihre klinische Bedeutung für die Erkennung der Hypofysengrösse. Fortschr. a. d. Geb. d. Röntgenstr. 49. 364—396 (1934).

Dibbern, H.: Ein Beitrag zur Röntgendiagnostik des Gehirns und seiner Hüllen. Fortschr. a. d. Geb. d. Röntgenstr. 52. 425—442 (1935).

Erdèlyi, J.: Die Röntgendiagnostik der Hypofysengeschwülste. Fortschr. a. d. Geb. d. Röntgenstr. 51. 125—147 (1935).

Farberow: Röntgendiagnostik der Tumoren der Gegend der Sella turcica. Fortschr. a. d. Geb. d. Röntgenstr. 50. 445—465 (1934).

Gilbert, R.: Les variations de forme et de grandeur de la selle turcique. Confinia Neurologica. 6. 157—161 (1934).

Haas, L.: Einzelheiten aus der Röntgendiagnostik der Sella turcica. Fortschr. a. d. Geb. d. Röntgenstr. 50. 465—469 (1934). 51. 147—152 (1935). 52. 186—188 (1935).

Heublein, G. W.: Some observations concerning the hypophysial fossa. Amer. Journ. of Roentg. 56. 299—319 (1946).

Greving, H.: Zur Differentialdiagnose krankhafter Veränderungen der Sella turcica im Röntgenbild. Nervenarzt. 13. 353—359 (1940).

Holm, O. Fr.: Über Heilungsphänomene in der Sella turcica nach Behandlung von intrasellären Tumoren. Acta Radiologica. XXIV. 495—510 (1943).

Klöppner, K.: Röntgenologische Studien an der Sella turcica bei Frauen. Zeitschr. f. Geburtshilfe u. Gynäkologie. 120. 41—70 (1939).

Kornblum, K.: Deformation of the sella turcica in tumors of the middle cranial fossa. Amer. Journ. of Roentg. 31. 23—30 (1934).

Kornblum, K. and Osmund, L.: Effect of intracranial tumors on the sella turcica. Arch. of Neurology and Psychiatr. 34. 111—123 (1935).

Lüdin, M.: Veränderungen der Sella turcica bei sellafernen intrakraniellen Tumoren. Acta Radiologica. XVI. 48—50 (1935).

Nichols, B.: The roentgenological diagnosis of tumors in the sellar region. Amer. Journ. of Roentg. 33. 733—735 (1935).

Pette, H.: Über Röntgenbefunde an der Sella turcica bei raumbeschränkenden Prozessen innerhalb der Schädelhöhle. Arch. für Psych. u. Nervenkrankheiten. 95. 772—773 (1931).

Scheuermann, H.: On the size and form of the sella turcica in the various pituitary adenomas. Acta psych. et neurol. 19. 347—365 (1944).

Schüller, A.: Röntgendiagnostik der Erkrankungen des Kopfes. Lehrbuch der Röntgendiagnostik von A. Schittenhelm. 124—227 (1924).

FROM THE ROENTGENDIAGNOSTIC DEPARTMENT OF KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN (CHIEF: PROF. Å. ÅKERLUND)

AXIAL PROJECTION OF THE GALL BLADDER[1]

by

K. Lindblom

Gas bubbles within the colon may disturb the study of the gall bladder, especially when films are taken with tbe patient in erect position. Even repeated enemas are not always able to empty the gas. The purpose of this paper is to demonstrate that a projection axial or almost axial to the long axis of the gall bladder is the simplest way to free this organ from overlapping gas.

The patient is roentgenographed in erect p—a position with forced lordosis, the lumbar spine being supported by a big pad (Fig. 1). A small anterior pad serves the compression of the gall bladder area. The rays are centered over this area and are directed horizontally.

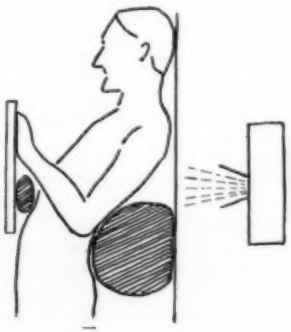


Fig. 1. Positioning in axial projection of the gall bladder.

In this axial projection the adjacent part of the transverse colon lies caudally to the gall bladder (Fig. 2 a—b) except for the few cases in

[1] Submitted for publication, Oct. 20, 1949.

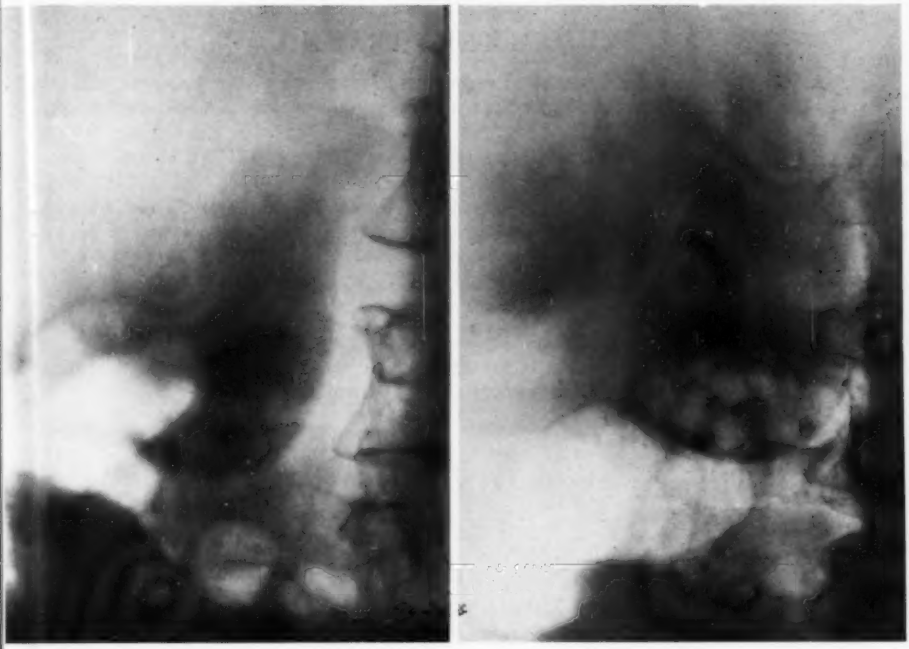


Fig. 2 a. Fig. 2 b.

Fig. 2 a—b. Roentgenograms of a gall bladder in erect position; usual and axial projections. Note that the transverse colon lies caudally to the gallbladder in the latter projection.

which the colon is interposed between the abdominal wall and the liver and gall bladder. In ordinary cases the gall bladder reaches the abdominal wall.

Obviously, the axial projection increases the possibility to visualize the stones in those gall bladders which do not fill with dye. The overlapping gas is absent and the layer of the stones becomes thicker in the direction of the rays.

SUMMARY

Axial projection of the gall bladder removes the overlapping of gas bubbles and increases the possibility to visualize stones in a gall bladder without contrast filling.

ZUSAMMENFASSUNG

Axiale Projektion der Gallenblase verhindert Überlagerung von Gasblasen und gibt vermehrte Möglichkeiten Steine in einer Gallenblase ohne Kontrastfüllung darzustellen.

RÉSUMÉ

La radiographie en projection axiale de la vésicule biliaire empêche les bulles gazeuses de se superposer à elle et augmente les possibilités de mettre en évidence des calculs du cholécyste non rempli de substance opacifiante.

FROM THE DEPARTMENT OF EXPERIMENTAL HISTOLOGY, KAROLINSKA INSTITUTET, STOCKHOLM, SWEDEN.

THE REACTION OF THE LUNG ON BRONCHOGRAPHY WITH VISCOUS UMBRADIL (UMBRADIL-VISKÖS B) (ASTRA), UMBRADIL (ASTRA), AND CARBOXYMETHYL CELLULOSE[1]

An experimental investigation on animals

by

B. Hellström and *Hj. Holmgren*

On using contrast media in bronchography it is naturally very important to know the reaction of the bronchial tree and the lungs to the contrast medium used. The substance should in the first place give a good contrast. It should also, as far as possible, remain in the part of the lung into which it is injected, cause the least possible degree of irritation to the lung and, finally, disappear as rapidly as possible. The present investigation was carried out in order to ascertain whether Umbradil-Viskös B (Astra) fulfils these requirements.

Judging from the literature no extensive and systematic investigations of this kind have been done. HUEPER's investigation (1945) on intravenous injection of sodium cellulose glycollate (Collacel S) is of interest in the present work. The substance was injected intravenously into five dogs. After single and repeated injections the animals were subjected to hematologic and pathologico-anatomic examinations. The separate organs and large vessels of those animals which had received daily injections for a long period were examined closely. The hematologic examination showed transient leukopenia, a decrease in hemoglobin and an increase in the sedimentation rate. In the examined organs HUEPER found a deposition of the injected matter in the reticulo-endothelial cells of the liver and spleen and in the glomerular endothelial cells and inter-

[1] Submitted for publication August 23, 1949. The investigation has been financed by A. B. Astra, Södertälje (Sweden).

stitial cells of the kidney. Further he found formation of atheromatous deposits in the aorta and its branches. In the tubular lumina of the kidney he found bluish staining casts with hematoxylin-eosin, indicating that the injected material was excreted through the kidney.

Material and Methods

In the experiments we used 130 large white rats and 17 rabbits. The rats were anesthetized with 2 % avertin solution intraperitoneally, the rabbits with 20 % urethane solution intravenously. After tracheotomy, a ureter catheter was introduced under roentgen control into the bronchial tree, in most cases into the bronchus of the right lower lobe. In the case of most of the rats about 0.10 ml per 100 g of body weight of Umbradil-Viskös B, Umbradil and Carboxymethyl Cellulose, respectively, was administered through the catheter. Some animals were given physiologic saline solution. The rabbits received Umbradil-Viskös B 0.05—0.07 ml per 100 g of body weight. The dosage in relation to body weight is considerably larger than the dosage used in man.

In all the cases the position of the catheter was seen clearly on screening, and, when viscous and pure Umbradil was used, the localization of the substance after injection. The animals were killed at different intervals after bronchography, varying from half an hour to three weeks.

The following organs were examined histologically:

1) Lung tissue from lobe into which the material had been injected.
2) The hilus area on the same side.
3) Lung tissue from the untreated lung, in most cases the apex.
4) The trachea (in some cases).
5) Liver.
6) Kidney.

All the preparations were fixed with Susa and stained according to the following scheme:

Lungs and trachea ..... Htx-eosin, Azan, Weigert-van Gieson, Toluidine blue.
Liver and kidney ..... Htx-eosin, Azan, Toluidine blue.

The Reactions Observed in the Experimental Animals after Injection

White rats.

Umbradil-Viskös B.

Ten out of 50 animals died after the injection. Six of these died immediately after bronchography and four after about one hour. In six cases death was probably caused by pure suffocation, as after the injection the substance regurgitated, partly passing out through the opening

n the trachea and partly being reaspirated, blocking up also the bronchial branches on the other side. It was therefore necessary to place the animals n vertical position for about one hour immediately after the injection. n the animals that died after about an hour or so, the regurgitated matter was foamier and thinner. The viscous Umbradil had evidently become more or less mixed and diluted with secretion from the mucous membrane.

Most of the surviving animals showed no distinct reaction. In some cases, however, there was dyspnea, and in a few cases transient apnea.

Umbradil.

Three out of 20 animals died in connection with the injection. Otherwise the reaction was on the whole the same as for rats treated with viscous Umbradil.

Carboxymethyl Cellulose.

None of the 15 treated animals died in connection with the injection. We observed no distinct reaction, with the exception of apnea of short duration in one animal.

Physiologic Saline Solution.

No reaction was observed.

Umbradil-Viskös B.

Three of the 17 treated animals died in connection with the anesthesia, three immediately after the injection and two $^1/_2$ to 1 hour after bronchography.

Also in the rabbits we observed secretion from the mucous membrane of the respiratory tract. In order to avoid suffocation also the rabbits had to be placed in vertical position for $^1/_2$ to 1 hour after the injection.

The general reaction of the rabbits was the same as in the rats. A remarkable fact is, however, that the general condition was affected to a greater extent in the rabbits than in the rats still after 24 hours, persistent dyspnea being one of the symptoms.

Macroscopic Changes

White rats.

Umbradil-Viskös B.

The lung into which the contrast medium was injected as well as the untreated lung will be described in the following.

Immediately after the injection the lung lobe concerned showed a dark bluish red colour, due to reduced air content, and the parenchyma was soaked with the viscous fluid. There did not appear to be any macro-

scopically observable increase in blood. Already after one hour or two the picture changed. The lobe concerned became richer in blood and the bronchial content thinner. In some cases the bronchial content spread to other lobes which then became the seat of similar, although less extensive changes. The picture remained the same still after 12—24 hours. The changes showed no sign of regression until after 24 hours. After 48 hours the lobe concerned showed, macroscopically, a normal picture on the whole, but the blood content varied. After 72 hours the macrosocpic picture was normal except in those few cases where a secondary infection had set in. Finally, with regard to the appearance after one to two weeks, the lobes presented macroscopically a fully normal picture.

The untreated lung appeared in most cases normal irrespective of the time relapsed after the injection. A few cases showed changes similar to those in the treated lung over limited areas. This fact suggests that small amounts of the injected material had regurgitated and been aspirated into the untreated lung.

Umbradil.

It may be summarized that pure Umbradil gives more marked and more extensive changes with more copious secretion, which in many cases involve both lungs. The reason for this may possibly be the absence of the viscous component which helps to bind the bronchial content to the treated lobe and side. Also with pure Umbradil the lung presents a fully normal picture after one to two weeks.

Carboxymethyl Cellulose.

The macroscopic changes in the treated lobe were the same as in the previous case. They were, however, more clearly defined and spread to the untreated lung only in one instance. Thus, carboxymethyl cellulose produces evidently macroscopic changes but on account of its high viscosity it is not aspirated to any great extent by other portions of the lung. After a week the treated lung presents macroscopically a fully normal picture.

Physiologic Saline Solution.

Macroscopically the treated lung presented on the whole a normal picture one to three hours after the injection. It showed, however, more or less marked hyperemia. The untreated lung presented a normal picture.

Umbradil Viskös B. Rabbits.

Already $^1/_2$ hour after the injection distinct macroscopic changes were observed in the lobe into which the material was injected. The changes

consisted in increased blood content, increased secretion and minor patches of atelectasis. This picture remained for the next few hours.

Microscopic Changes

In the cases where the trachea was examined we were not able to observe any noteworthy changes. On microscopic examination of the lungs the changes were found to involve principally certain structural elements:

The alveolar content. We have tried to estimate as far as possible the amount and the nature of the alveolar content.

Blood content. As it is extremely difficult to estimate the blood content of the lung from the histologic picture particularly with regard to the normal accumulation of blood in the vascular sinus (see SJÖSTRAND 1938), we have only been able to state whether the blood content of the lung has appeared to be obviously increased or not.

Alveolar septa. We have considered that a thickening of the septa indicates a pathologic irritation. In some cases the thickening has advanced so far that the alveolar character of the lung is nearly obliterated. It should be pointed out, however, that thickened septa are sometimes found in untreated »normal» lungs from rats. In those cases where we observed no other changes than thickened septa we did not attach much importance to the latter.

Leukocytes and round cells. In lungs of rats there are normally accumulations, particularly peribronchially, of lymphocytes. We have tried to investigate to what extent these were increased and whether a leukocyte infiltration could be observed as a sign of foreign-body irritation or infection.

Alveolar phagocytes. As it was found at an early stage that certain cellular elements in the lung had a phagocytic action on carboxymethylcellulose we have, in particular, followed and observed the changes in these cells and the quantity of phagocytosed matter that they contained. In the group alveolar phagocytes we have included all the cells in the lung tissue, which showed clear phagocytosis. Thus, this would include partly true phagocytes, partly alveolar epithelium. The latter possesses phagocytic ability, at least in cultures according to TIMOFEJEWESKY and BENELOWENSKAYA (1925).

White rats.
Rabbits.

Umbradil-Viskös B.

Before describing the observed changes we will give a brief account of the staining of Umbradil-Viskös B (U. V.), according to the histologic methods used by us. With Htx-eosin, U. V. appeared in the alveoli

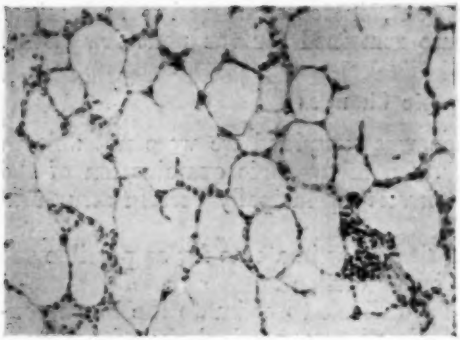


Fig. 1 a.

Untreated lung from rat. Thin alveolar septa.
Staining: Htx-eosin. 142 ×.

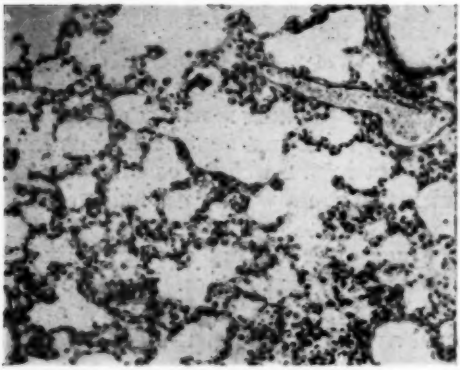


Fig. 1 b.

Lung tissue from lobe after injection of Umbradil-Viskös B. The animal was killed after 1 hour. Copious alveolar content which has not stained. Thickened septa and enlarged alveolar phagocytes.
Staining: Htx-eosin. 142 ×.

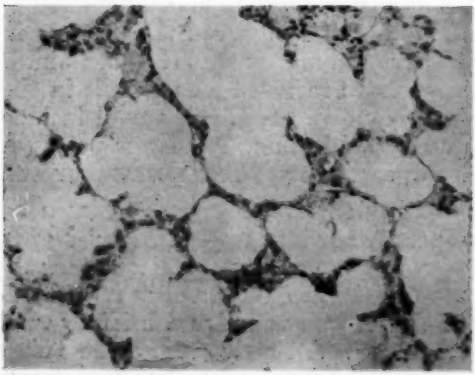


Fig. 1 c.

Lung from rat killed 72 hours after injection of Umbradil-Viskös B. The changes are on the return, but the septa are still slightly thickened.
Staining: Htx-eosin. 142 ×.

Fig. 2 a.

Lung from rat after injection of Carboxymethyl cellulose. The animal was killed after 24 hours. The alveoli almost completely filled with a content which has stained well.
Staining: Toluidine blue. 142×.

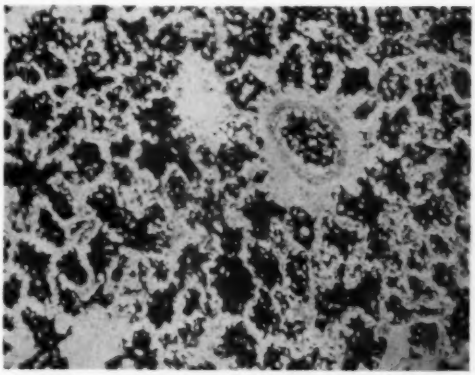


Fig. 2 b.

Lung from rat after injection of Umbradil-Viskös B. The animal was killed after 48 hours. Sparse content in the alveoli. Thickened septa with numerous alveolar phagocytes distinctly observable on account of their ingested content.
Staining: Toluidine blue. 142×.

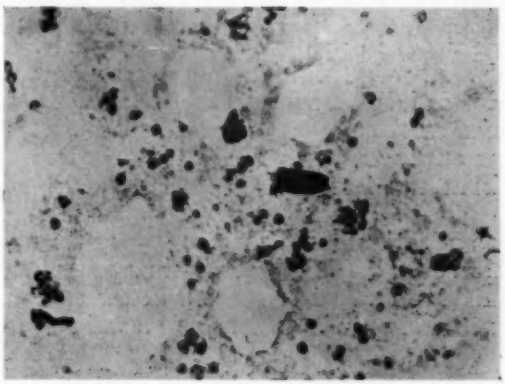
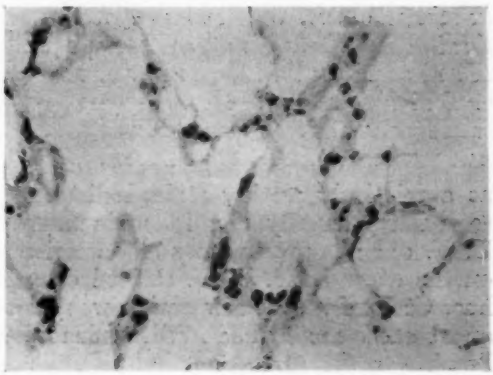


Fig. 2 c.

Lung from rat after injection of Umbradil-Viskös B. The animal was killed after 72 hours. The septa only slightly thickened; numerous alveolar phagocytes with abundant content.
Staining: Toluidine blue. 142×.



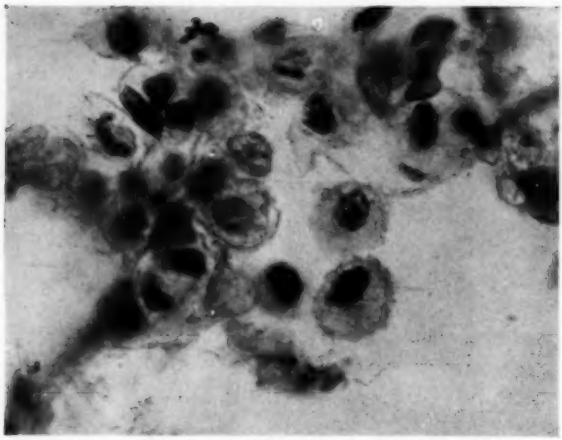


Fig. 3 a.

Enlargement of fig. 1 b. Enlarged alveolar phagocytes without staining inclusions in the cytoplasm.
Staining: Htx-eosin.
1,100 ×.

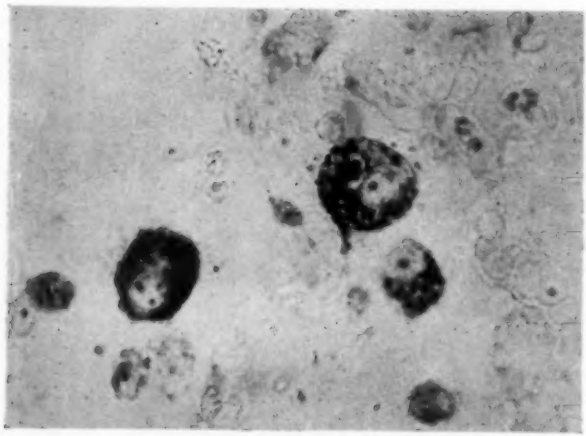


Fig. 3 b.

Enlargement of fig. 2 b. The enlarged alveolar phagocytes contain an abundance of readily stainable granules.
Staining: Toluidine blue.
1,100 ×.

as a relatively weakly stained dirty red mass, which on addition of secretion gradually lost its stainability. With van Gieson and Azan U. V. did not present any characteristic picture. With toluidine blue on the other hand, U. V. stained deep dark blue with a bluish violet hue. Gradually as the secretion was added the colour lost its intensity and became more violet. This stainability is characteristic and is attributable to the carboxymethyl cellulose component. As the parenchyma

stains only light blue the alveolar content appears in sharp contrast with this mode of staining.

Half an hour to three hours after bronchography the alveoli were filled with a content that stained readily with toluidine blue but was gradually diluted with the addition of secretion. The septa became thicker and the blood content was increased simultaneously (fig. 1 b). The alveolar phagocytes began to grow larger. Their cytoplasma was swollen and of a slightly foamy appearance (fig. 3 a). There were no observable signs of phagocytosis. The leukocyte content was seemingly normal. After three hours the untreated lung began to show slight changes, having appeared fully normal until then.

After six hours the changes in the affected part of the lung became more pronounced; in some cases the alveolar structure was obliterated. Fine granules with the same stainability as the alveolar content were now observed in the alveolar phagocytes.

Twelve to twenty-four hours after bronchography the septa still showed distinct changes and the blood and leukocyte content was markedly increased. The alveolar phagocytes were further enlarged and contained a large quantity of ingested matter. Also in untreated portions of the lung slight changes were observed in some cases, *e. g.* enlarged phagocytes containing sparse ingested granules.

The changes began to subside slowly after 24 hours and in the animals killed 48 hours after bronchography the content was much sparser than in the 24 hour animals (fig. 2 b and 3 b). Remnants of the alveolar content were found also in the 72 hour animals (fig. 2 c), but in these as well as in the 48 hour animals the blood content was on the whole normalized. The septa were thickened in all the cases (fig. 1 c) and the leukocyte content varied from case to case, in some instances it was fully normal. The alveolar phagocytes were still enlarged and contained a varying number of granules. In the animals killed one week after bronchography the alveoli still contained fine remnants of a content readily stainable with toluidine blue. Other changes were of a very varying nature; the granular content of the alveolar phagocytes varied also. After two weeks there were almost in every case no free granules in the alveoli and no noticeable increase in the blood content or the number of leukocytes. A remarkable fact is that the septa now began to resume a normal appearance, whereas the alveolar phagocytes, on the other hand, still contained varying amounts of granules. The untreated lung in the 1 to 2 week animals showed on the whole a normal picture. The animals killed three weeks after bronchoscopy presented on the whole a normal picture, the only change being a slight thickening of the septa. The alveolar phagocytes, however, contained a sparse amount of ingested matter.

Umbradil.

With regard to the stainability Umbradil (U.) showed no characteristic tint after staining with hematoxylin-eosin, van Gieson and Azan. With toluidine blue it stained extremely weak blue.

Abundant alveolar content was observed in the animals killed one hour after bronchoscopy. The blood content was considerably increased, the leukocyte content, on the other hand, was normal. The septa were thickened and the alveolar phagocytes were enlarged with a light, slightly foamy cytoplasm. The alveoli of the untreated lung contained in most cases a considerable amount of ingested matter and showed slight changes in the parenchyma.

In animals killed three hours after the injection the alveolar content was sparser. Most of the injected matter had evidently been already absorbed. Otherwise this group showed the same changes as the above-described group.

In animals killed 6—12 hours after the injection into the bronchial tree the alveolar content was sparse. Otherwise the picture was unchanged, except for an increase in the leukocyte content. The untreated lung appeared in most cases fully normal.

The picture remained unchanged on the whole still after 24 hours. In the cases which we examined a week after the injection the lungs appeared normal on the whole. A remarkable fact is that in no case were we able to demonstrate any granular phagocytosis whatsoever of the alveolar phagocytes in the experiments with pure Umbradil.

Carboxymethyl Cellulose.

Carboxymethyl cellulose (CMC) has the same tinctorial properties as U. V. A copious alveolar content was observed after half an hour. The septa showed some degree of thickening and the blood content was markedly increased. The alveolar phagocytes were changed, they were markedly enlarged and contained in some cases a few small blue granules.

Animals killed three hours after the injection showed changes of the same nature and extent as those described above. The untreated lung from animals belonging to this group was fully normal.

After 6—12 hours the changes had advanced. The septa were much thicker and in many cases the alveolar structure was entirely deranged. The blood content was increased or normal. In some cases the leukocyte content was also increased. The phagocytes were large and showed distinct phagocytosis. The untreated lung showed as a rule no great changes.

After 24 hours the alveolar content was still copious (fig. 2 a). Otherwise there were no further changes, except for an increase in the ingested

content of the phagocytes. There were no signs of spreading to the untreated lung.

A week after the injection the picture was almost normal but in some cases we found phagocytes containing a varying number of granules.

Physiologic Saline Solution.

Physiologic saline solution was injected into the bronchi in the same manner as the other substances. The experiments were made in order to find out to which extent the observed changes with U. V., U and CMC are to be regarded as unspecific and as being a reaction to foreign bronchial content on the whole. It was found that the lung showed changes similar to those we had obtained in experiments with the other substances described here. Thus, the septa were thickened, the blood content increased and the alveolar phagocytes were enlarged. Except for varying degrees of hyperemia, the macroscopic finding was normal.

The Microscopic Picture of Other Examined Organs

White rats.
Rabbits.

Kidneys.

Umbradil-Viskös B, Umbradil and Carboxymethyl Cellulose.

With regard to the histologic picture of the kidneys no certain pathologic changes were observed. In the cells of the renal tubules and in the lumina, however, we found various-sized bluish green granules staining with toluidine blue. We have not found these inclusions in normal animals. But as they occurred whether U. V., U. or CMC was injected, the appearance of the inclusions cannot be associated with the injected materials or their decomposition products. The inclusions do not seem to appear until after a few hours.

Liver.

We have observed no changes in the liver, which may be associated with the media used in bronchography.

Discussion

The most important questions in this connection are probably the following:

1. Does the contrast medium as such or its components cause changes in the lungs, characteristic or unspecific?
2. Are the demonstrated changes persistent or of a temporary nature?

3. Are the changes of such a character that they may cause severe functional disturbances while they last?

4. Does the present investigation furnish any evidence as to whether and in what way the CMC component influences the general and the histologic reaction?

An injection into the bronchial tree is naturally under any circumstances an intervention, which is bound to leave traces in a tissue as sensitive as the lung parenchyma. It should be pointed out that the large bronchi are lined with ciliated epithelium with goblet cells, whereas the small bronchi are lined with finer epithelium. A mucous membrane of this character must naturally be very vulnerable. The alveolar components should be still more readily damaged. These consist of alveolar epithelium and, according to most authors, of a thin layer of cytoplasm which separates the alveolar air from the capillary. In the septa which form the alveolar walls there are, besides capillaries, normally free leukocytes and the so-called septal cells, whose origin appears to be obscure. Some authors consider that septal cells possess phagocytic ability, while others repudiate this. In the lung septa there are also free phagocytes. Finally, the alveolar wall consists of a relatively sparse principally elastic, connective tissue. As already mentioned in the lungs of rats there are relatively abundant accumulations of lymphocytes, particularly in the hilus area.

From the foregoing it is clear that the lung with its structure of naked well-differentiated cells, must be very vulnerable. At the same time the structure of the parenchyma is such that certain definite reactions after stimulation may be expected from it.

With the large dosis used in our experiments a relatively great number of the animals died in connection with the injection of U. V. and U., whereas no animals died after injection of CMC. This is probably due to the fact that U. V. and U. cause a more marked irritation of the mucous membrane than CMC. The more copious secretion in the case of U. V. and U. causes regurgitation and reaspiration, with suffocation as the result. CMC does not seem to have the same irritating effect on the mucous membrane and owing to its high viscosity it does not regurgitate so readily and does not spread to other parts of the lung. The assumption that CMC does not to any remarkable degree stimulate secretion is borne out by the fact that remnants of undiluted CMC may be found in the alveoli a week after injection of U. V. By that time the U. has already been absorbed. Despite the different effect of the substances on the mucous membrane the latter does not in our preparations differ markedly from the normal mucous membrane.

1. The changes in the lung which we have observed macroscopically as well as microscopically are on the whole of the same appearance with

all the injected substances. The extent of the changes depends altogether on the viscosity of the injected matter. As also physiologic saline solution produces changes of the same nature as those caused by the other substances used, although not so marked, we consider that the observed changes are of an unspecific nature. Nearly all the changes seem to appear during the first half hour after injection, which suggests that most of the cellular elements of the lung are from the beginning engaged in the reaction of the lung. Only the leukocytic mechanism does not seem to function until later. An interesting fact is that the alveolar phagocytes, in which we include also all cells that show phagocytosis, are obviously involved already before the actual phagocytosis has started. Distinct signs of phagocytosis are not noticed until after one hour, when they have ingested the CMC. In experiments with only U., they are much enlarged but contain no granules indicating phagocytosis. The reason for this may be either that the U. does not stain after phagocytosis or that the injected matter is diluted with the secretion, whereupon it is absorbed and carried away via the blood. The latter seems to be the more probable explanation.

In the cases which received U. V. or CMC, the phagocytes were not seldom found to accumulate in large groups. In some cases we found also large multinuclear cell elements which were probably changed phagocytes. These would probably correspond to the giant-syncytia of dust cells in the lungs of guinea pigs described by WESLAU (1934).

Owing to its high viscosity, CMC stays along the bronchial and alveolar walls and it remains in the alveolus in a rather concentrated form. Because of this and of the comparatively large molecule of CMC the substance is probably not absorbed directly, but is first ingested by the alveolar phagocytes, whereupon it is either split inside these or passes out into the blood. In any case there are probably different ways of absorption of U. and CMC.

2. The observed changes are certainly deep-going, in some cases the alveolar mechanism is entirely blotted out. The investigation has shown, however, that the changes subside gradually. The increased blood content and the leukocytic reaction seem to become normalized first. The other changes disappear much more slowly. Judging from the preparations the alveolar phagocytes are probably the last cellular elements to become normalized.

From all indications the changes produced by the injection are of a reversible nature.

3. In the beginning the changes have undoubtedly a damaging effect on the functions. When the alveolar content has been absorbed the organ should be able to function satisfactorily again. The thickening of the septa, however, which persists for a relatively long time, may to some

extent have a lowering effect on the functions. Also CMC stays in the lung longer than U. and spreads to the alveolar wall, which may render the exchange of gases difficult.

The changes of the lungs are of such a nature that they may cause a temporary lowering of the function in the affected area.

4. We have found that the secondary changes in the lung are more marked and appear over larger areas when U. is used than when CMC is used.

This fact together with the tendency of CMC to stimulate secretion to a lesser degree than U. suggests that the addition of CMC is an advantage in the respect that the changes are largely restricted to the lobe into which the injection is made.

SUMMARY

In experiments with rats and rabbits the authors have studied the reaction of the lungs on injection into the bronchial tree of Umbradil-Viskös B (Astra) and its components. With screening as a means of control a ureter catheter was, after tracheotomy, introduced as a rule into the bronchus of the right lower lobe. The dosage in relation to the body weight was considerably larger than the dosage in man. Histologically, changes were demonstrated which seemed, principally, to be of an unspecific nature and which were also produced on injection with physiologic saline solution. From all indications, there are different ways for the excretion of the components of Umbradil-Viskös B. Umbradil seems to be absorbed directly, whereas carboxymethyl cellulose on the other hand is ingested by the alveolar phagocytes, in which, owing to its marked affinity for toluidine blue, the substance may be demonstrated as granular inclusions. The alveolar content disappears after a week or two and the histologic changes manifested in *e. g.* thickened septa and increased blood content, have started to subside already earlier. After a few weeks the picture is on the whole normal.

ZUSAMMENFASSUNG

In Versuchen mit Ratten und Kaninchen haben wir die Reaktion der Lungen auf Einspritzung von Umbradil-Viskös B (Astra) und seinen Komponenten in den Bronchialbaum studiert. Unter Durchleuchtungskontrolle wurde ein Ureterenkatheter nach Tracheotomie zumeist in den Bronchus des rechten Unterlappens eingeführt. Die Dosierung im Verhältnis zum Körpergewicht lag bedeutend höher als die Dosierung beim Menschen. Histologisch wurden Veränderungen nachgewiesen, die vorwiegend unspezifischer Natur zu sein schienen und auch durch Einspritzung von physiologischer Kochsalzlösung hervorgerufen wurden. Allem Anschein nach gibt es verschiedene Wege der Ausscheidung der Komponenten von Umbradil-Viskös B. Umbradil scheint direkt absorbiert zu werden, während andrerseits die Karboxymethylzellulose von den Phagozyten der Alveolen aufgenommen wird, in denen die Substanz, dank ihrer ausgesprochenen Affinität zu Toluidinblau, als körnige Einlagerungen nachgewiesen werden kann. Dieser Alveolarinhalt verschwindet nach einer bis zwei Wochen, und die histologischen Veränderungen, die sich z. B. als Verdickung der Septen und vermehrter Blutinhalt zu erkennen geben, haben schon früher angefangen zurückzugehen. Nach wenigen Wochen ist das Bild im grossen ganzen normal.

RÉSUMÉ

Par des expériences sur des rats et des lapins les auteurs ont étudié comment les poumons réagissent à l'injection, dans l'arbre bronchique, d'Umbradil Visqueux B (Astra) et de ses composants. Sous le contrôle de la rœntgenoscopie on a introduit, après trachéotomie, une sonde uretérale atteignant, dans la règle, la bronche du lobe inférieur droit. Le dosage, par rapport au poids du corps, était considérablement plus élevé que chez l'homme. Histologiquement on a mis en évidence des lésions qui semblaient être avant tout de caractère non spécifique et qu'on produisait aussi en injectant du sérum salé physiologique. Tout indique qu'il existe diverses voies d'excrétion des composants de l'Umbradil Visqueux B. L'Umbradil semble être absorbé directement, tandis qu'en revanche la cellulose carboxyméthylique est ingérée par les phagocytes alvéolaires au sein desquels cette substance, grâce à son affinité marquée pour le bleu de toluidine, peut être rendue visible sous la forme d'inclusions granuleuses. Le contenu des alvéoles disparaît après une semaine ou deux, et les altérations histologiques, se manifestant par ex. sous la forme d'un épaississement des cloisons ou sous celle d'une hyperémie, ont commencé à rétrocéder encore plus tôt. Au bout de peu de semaines l'image, à tout prendre, est normale.

REFERENCES

HUEPER, W. C.: Amer. Journ. of Path. 21: 1021 (1945).

SJÖSTRAND, F. and SJÖSTRAND, T.: Anat. Anz. 87: 193—256 (1938).

TIMOFEJEWESKY, A. and BENELOWENSKAYA, S.: Virchow's Arch. 255: 613 (1925).

WESŁAW, W.: Contribution à l'histophysiologie et l'histopathologie de l'épithélium pulmonaire des vertébrés. Posen 1934.

FROM THE I. ROENTGENDIAGNOSTIC DEPARTMENT OF SÖDERSJUKHUSET, STOCKHOLM, SWEDEN (CHIEF: DOCENT G. JÖNSSON)
In cooperation with the II. Medical Clinic of Södersjukhuset, Stockholm (Chief: Prof. G. NYLIN)

SELECTIVE ANGIOCARDIOGRAPHY[1]

by

Gunnar Jönsson, Bror Brodén and *Johan Karnell*

The method of angiocardiography described by CASTELLANOS, PEREIRAS and GARCIA and modified by ROBB and STEINBERG has the disadvantage that the contrast medium must travel a long distance before it reaches the vessel or part of the heart to be examined. The result is that it is often so diluted when it reaches its destination that no pictures of any use can be taken (fig. 5). In order to reduce this disadvantage, CHAVEZ, DORBECKER and CELIS made a modification in the technique. Instead of using a cubital vein, they inject the contrast solution into the right auricle or the right ventricle via a catheter inserted through the jugular vein. This eliminates the passage through the mediastinal veins and results in denser shadows. For the same purpose ROUSTHÖI and RADNER suggested arterial catheterization and injection of the dye into the thoracic aorta when this vessel is to be studied. The clinical use of this method was described by BRODÉN, HANSON, JÖNSSON and KARNELL.

Small children can be examined quite satisfactorily with ROBB's and STEINBERG's method. Similarly it often gives distinct pictures of the cardiac chambers and great vessels in adults when there are no abnormal changes. *Its drawbacks become apparent, however, on the examination of older children and adults with abnormal changes in the intrathoracic circulation.* The rest of this article is only concerned with the latter category.

Position of the patient. According to the original technique, the patient is examined sitting down. The dye is injected in the arm, lifted up to form

[1] Read at the meeting of the Northern Association for Medical Radiology, Stockholm June 10—12, 1949; submitted for publication, Oct. 1, 1949.

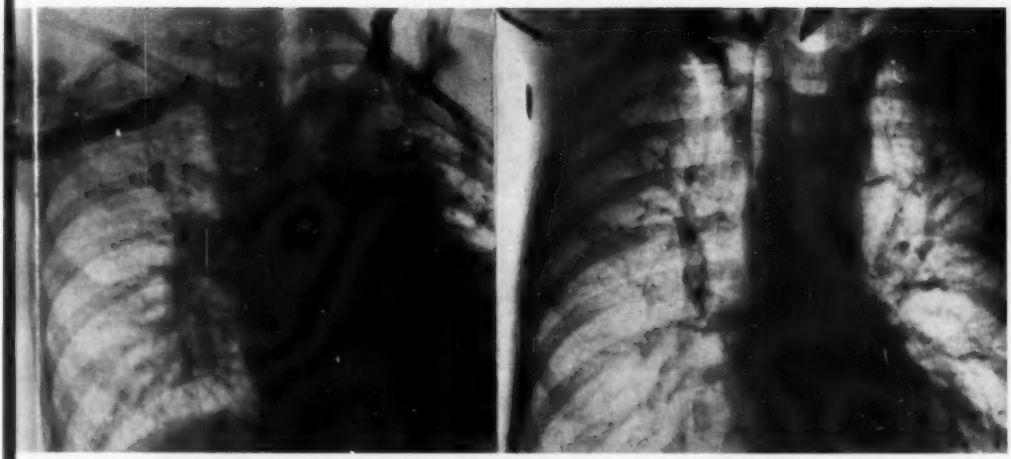


Fig. 1. Fig. 2.

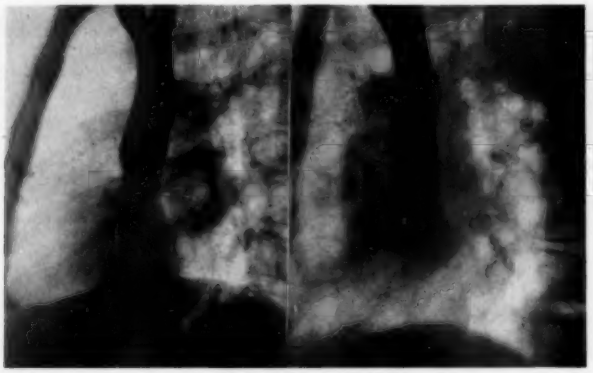
Fig. 1. Male aged 7. Coarctation of the aorta. The patient lying on his back. The contrast solution was injected in a cubital vein on the right side. A large amount of the solution has remained in the subclavian vein. The dye is also spread throughout the whole thoracic circulation so that the different details obscure one another. The picture was taken about four seconds after the injection. Forty cc. of a 70 per cent solution of diodrast were injected in about two seconds.

Fig. 2. Same patient as in figure 1 lying on his left side. The contrast solution was injected in a cubital vein on the right side with the arm held vertically. The solution has passed through much more quickly than in figure 1. Both pictures were taken about four seconds after the injection. Thirty-five cc. of a 70 per cent diodrast solution were injected in about three seconds.

an angle of at least 45 degrees with the horizontal plane. This position causes the dye to flow rapidly through the veins of the arm and superior vena cava down to the heart. In our opinion, however, it is better to have the patient lying down. In the first place, he is then under better control in case of accident. Secondly, we often use general anesthesia, always for children and for pictures of the left side of the heart or aorta, and more and more often for other cases as well.

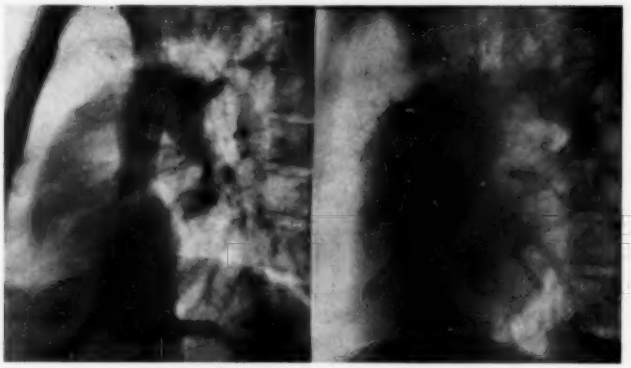
When the patient lies on his back, however, the contrast medium runs far too slowly through the veins in the arm and mediastinum (fig. 1), and a pool of dye collects in the lowest part of the passage, the subclavian vein. The loss of contrast medium there is not so important. The worst is that the opaque substance keeps on oozing into the circulating blood. Thus the right side of the heart and pulmonary vessels are never

Fig. 3 a¹ Fig. 3 b¹



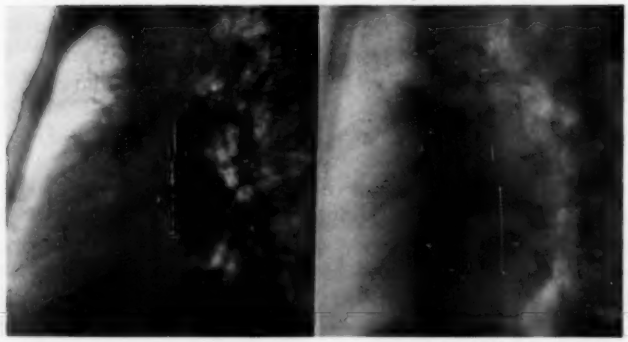
2 seconds after the injection.

Fig. 3 a² Fig. 3 b²



5 seconds after the injection.

Fig. 3 a³ Fig. 3 b³



11 seconds after the injection.

rid of it during the time the series of pictures are taken and still contain some when the left side of the heart and aorta are best filled. If the patient lies on his side and his arm is held vertically, the dye travels at a much faster rate (fig. 2). It is awkward to have the patient in this position, however, especially for the anesthetist. We decided, therefore, in favour of the supine position. But this position requires special measures to ensure the dye arriving rapidly at the heart and central vessels. *Our method is to inject the contrast solution through a catheter with the aid of a pressure apparatus.*

Projections. In accordance with ordinary roentgenologic principles, *pictures should be taken in at least two planes at right angles to one another.* In some cases it would be good to have other projections as well, but at present it is not possible to use more than two during one injection, and we do not like to inject the dye more than once. We have found that the two projections which give most informations are the purely frontal and purely lateral. We use these two almost exclusively now, but it would be wrong to make this a hard and fast rule. It should naturally be possible to vary this point in the procedure to suit the problem on hand.

Position of the catheter. In some cases the problem to be solved is more *physiologic* than anatomic. What is wanted is a rough idea of the rate the blood passes through the heart. Then the catheter should be placed in the superior vena cava, or the dye can be injected directly into a cubital vein in the manner of ROBB and STEINBERG. This question arises in the case of pericardiac constriction, for example. It may be that conclusive proof of this diagnosis can be gained from the angiocardiographic observation of an abnormally slow passage (fig. 3).

Fig. 3. Male aged 44. Pericardiac constriction, a) before and b) after pericardiolysis. Lateral view. Before the operation the blood circulated extremely slowly through the heart. Five seconds after the injection most of the contrast fluid is still left in the right auricle, the superior and inferior vena cava and their branches. Eleven seconds after, the solution has passed to the whole right side of the heart and pulmonary vessels, but has still not reached the left side of the heart. After pericardiolysis the circulation became more rapid. Five seconds after the injection the right side of the heart and pulmonary vessels are filled with contrast solution and eleven seconds after the solution is seen in the left part of the heart and aorta. Even so, the circulation is still slower than normal.

At both examinations 50 cc. of a 70 per cent diodrast solution were injected in a cubital vein on the left side, the injection taking slightly under two seconds. The patient was lying on his right side.

Fig. 4. Female aged 22. Tetralogy of Fallot after operation according to Blalock-Taussig. The tip of the catheter, inserted through the vena saphena magna upward through the inferior vena cava, has entered the left auricle. The fluid injected there does not go over to the right auricle. Nor did blood analysis show any signs of a shunt from the left to the right auricle. The catheter must have gone through the foramen ovale, though there was no auricular septal defect in the clinical sense. The left auricle and ventricle, the aorta and the anastomosis (arrow) to the pulmonary artery are visualized. Fifty-five cc. of a 70 per cent umbradil solution were injected in four seconds.

When it is a question of studying *anatomic* changes, the technique should be guided by another principle. Then, as a rule, it is only desired to see relatively limited areas and a disadvantage to have other parts of the circulation filled with dye. It is not possible entirely to avoid the latter, *but the aim should be to have the dye filling restricted as much as possible to the cardiac chamber and vessels of interest in the particular case.* Furthermore, the contrast solution should fill out the lumen in as concentrated form as possible. These requirements are best met if the catheter is placed so that its tip comes to lie in the chamber or vessel to be examined. The parts of the intrathoracic circulation for which this technique is feasible are the right auricle and ventricle, pulmonary artery and aorta.

In our material the *right auricle* has been of no great interest from an angiocardiographic point of view. The only malformation of importance which occurs there, the septal defect, is not visualized by filling the auricle with contrast fluid, unless it causes a shunt from right to left. Sometimes, however, it is possible to insert the catheter into the left auricle and in this way establish the diagnosis roentgenologically. This happened in slightly more than half our cases. It must be remembered, however,

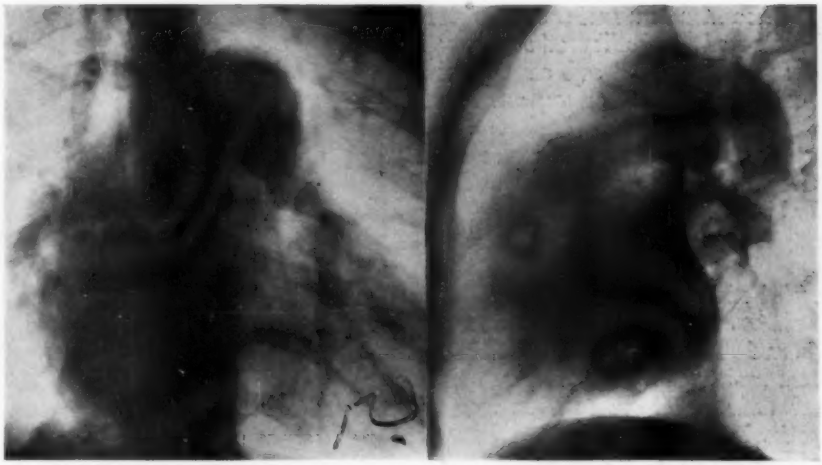


Fig. 5 a. Fig. 5 b.

Fig. 5. Female aged 26. Pulmonary stenosis. Frontal and lateral views. Injection of contrast medium according to Robb and Steinberg. The frontal picture shows a dense shadow of contrast medium in the right auricle and pulmonary artery. The density is less in the right ventricle, especially in the pulmonary conus. In the lateral picture the dye-filled right auricle, especially the appendage, is projected over the pulmonary conus, making it impossible to study any details there.

that the catheter can go through an open foramen ovale without there being a septal defect in the clinical sense, *i. e.*, a shunt. The injection of dye through a catheter in the left auricle may show whether or not there is a shunt (fig. 4).

It is much more important to be able to get distinct pictures of the *right ventricle*. There are situated some of the most common congenital malformations, *i. e.*, the different forms of pulmonary stenosis and transposition of the aorta. The ideal position for the tip of the catheter, would be in the centre of the ventricle proper. This wish, however, is often difficult to realize with the technique we use. The catheter tends to straighten out under the pressure of the injection, drawing the tip back up in the auricle. This would probably not happen if the catheter were inserted through the jugular vein, but we prefer to use a cubital vein for various reasons.

The catheter should be of as wide bore as possible. The wider the bore, the lower the pressure can be kept in the catheter and the less chance there is of its tip being dislocated. Another advantage of a wide caliber is that the dye does not flow so rapidly into the chamber — a point of

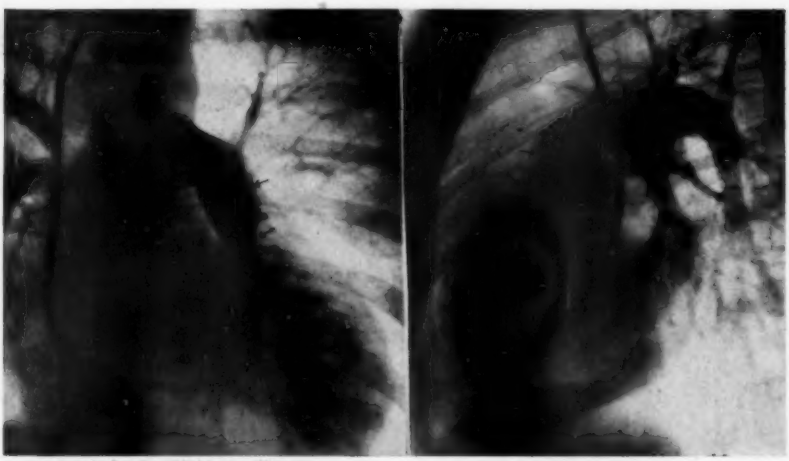


Fig. 6 a. Fig. 6 b.

Fig. 6. Female aged 14. Tetralogy of Fallot. Frontal and lateral views. The dye was injected through a catheter directly into the right ventricle. The right auricle being free of contrast fluid, every detail of the pulmonary conus is seen both in the frontal and lateral views. The lower arrow points to the infundibular stenosis, the upper one to the region of the pulmonary valves. Fifty cc. of a 70 per cent diodrast solution were injected in two seconds.

great importance. The muscles of the ventricular wall are highly sensitive to mechanical irritation, the touch of the soft tip of the catheter being enough to produce extra-systoles. A strong jet of fluid probably has the same effect, for electrocardiograms taken during the injection always show extra-systoles. Furthermore, the cardiac muscles are relatively fragile, and experiments we made on cadavers showed that the contrast fluid was pressed into the myocardium when it was injected too strongly. The catheter should not be finer than number 9 F, it may be that number 8 F can be used. Three or four seconds is about the right amount of time for the injection of 50 to 70 cc. (figs. 6, 7 and 8).

As yet no satisfactory method has been elaborated for detailed examination of the *left auricle and ventricle*. Occasionally it is possible to insert a catheter down into the left ventricle from the aorta but this is no basis for a routine technique. Furthermore, changes in the left side of the heart are not yet accessible to radical therapy. There is no real justification, therefore, for subjecting patients with this type of change to arterial catheterization, which after all is a serious undertaking. Septal defects can be reliably diagnosed with clinical methods and the same is true of

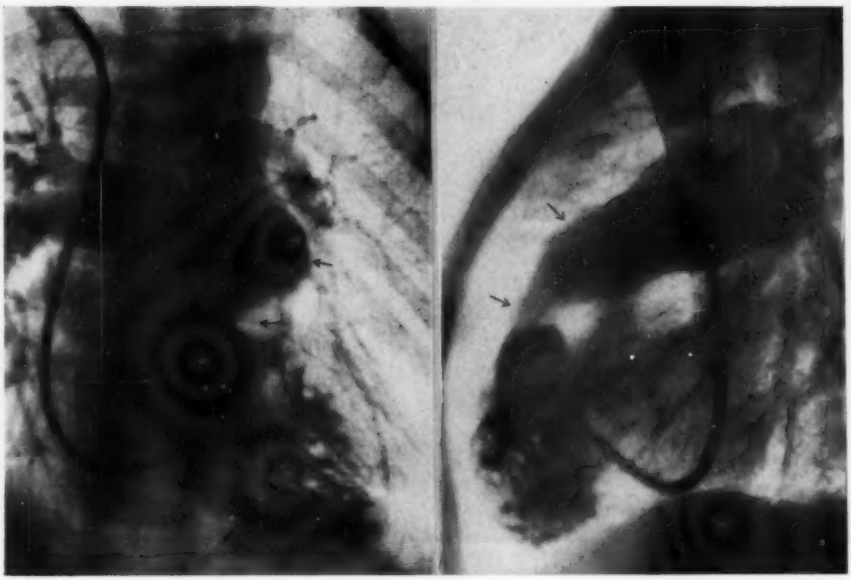


Fig. 7 a. Fig. 7 b.

Fig. 7. Male aged 11. Tetralogy of Fallot. Frontal and lateral views. Same technique as used for figure 6. The tip of the catheter lay in the right ventricle. The lower arrow points to the infundibular stenosis, the upper one to the region of the pulmonary valves. Forty-five cc. of a 70 per cent umbradil solution were injected in three seconds.

valvular disease. It may be that the diagnosis of congenital aortic and subaortic stenosis can sometimes be facilitated by the use of angiocardiography. As regards our technique of visualizing the left auricle and ventricle, we inject the contrast solution as rapidly as possible with the catheter lying in the pulmonary artery to avoid it becoming diluted with the blood in the right auricle and ventricle. We have obtained fairly clear pictures with this method. But just as good ones are sometimes obtained with ROBB's and STEINBERG's original technique, and we have not yet had enough experience to say whether injection in the pulmonary artery is any real improvement (fig. 9). As mentioned before, we use general anesthesia for examination of the left auricle and ventricle. Otherwise there is a risk that the patient begins to cough when the dye passes through the lungs, destroying every chance of distinct pictures. This is just as true of intravenous injection as of injection in the pulmonary artery.

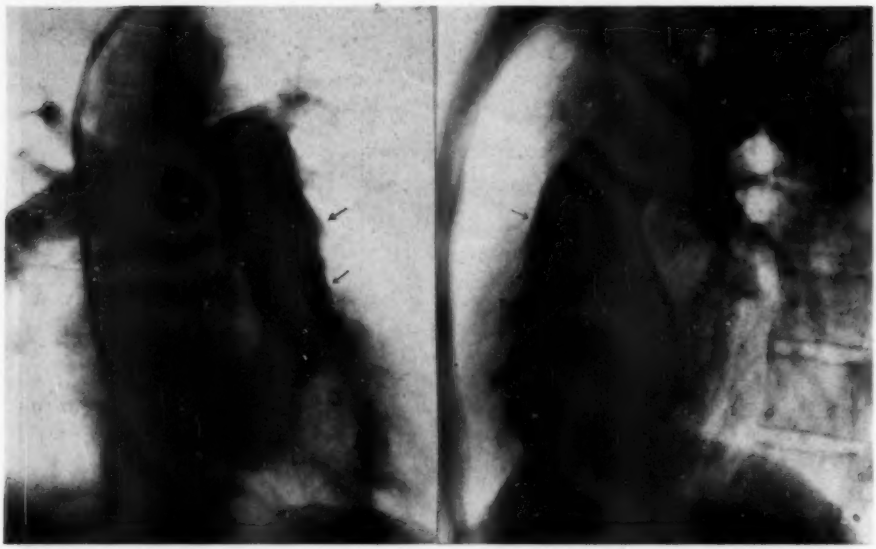


Fig. 8 a. Fig. 8 b.

Fig. 8. Female aged 38. Eisenmenger's complex. Frontal and lateral views. The contrast solution was injected through a catheter directly into the right ventricle. There is no opaque substance in the neighbourhood to obscure the pulmonary conus, indicated by lower arrow. No stenosis. The upper arrow points to the region of the pulmonary valves. 60 cc. of a 70 per cent solution were injected in 3 seconds.

We use the same technique for *examination of the aorta when one or another condition makes it impossible to inject the dye directly through the arterial system*. Direct aortography gives better results, however, the same rule applying to the aorta as the other vessels or the cardiac chambers: *In order to get distinct pictures the contrast medium must be injected directly into the lumen it is desired to study.*

It is much easier with our method than the original, standardized and rigid method of ROBB and STEINBERG *to take advantage of situations arising during catheterization for clinical purposes, i. e.*, for measurement of pressure and blood gas analysis. Thus, even when it is not originally intended to combine the catheterization with contrast studies, the instruments needed for these studies should always be kept in readiness (fig. 10).

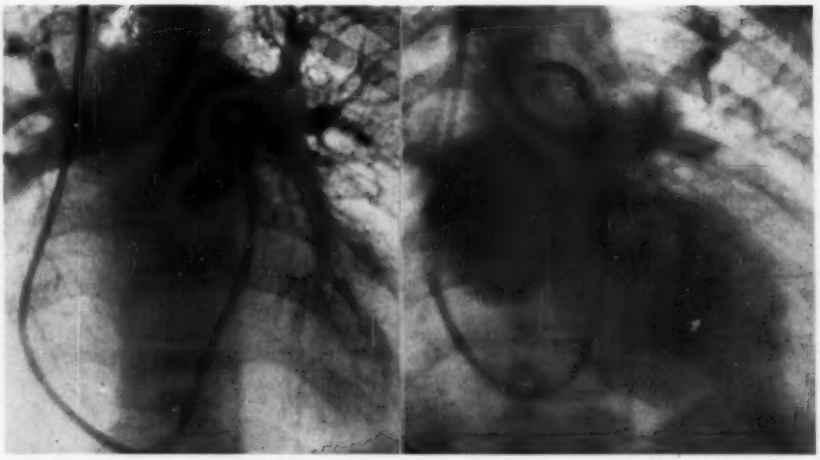


Fig. 9 a. Fig. 9 b.

Fig. 9. Male aged 17. Aortic stenosis. The dye was injected through a catheter in the pulmonary artery (a). A few seconds later the left auricle and ventricle were clearly visualized (b). Sixty cc. of a 70 per cent umbradil solution were injected in about two seconds.

Scheme for Selective Visualization of the Chambers of the Heart and the Great Vessels

Forty to 70 cc. of a 70 per cent umbradil (diodrast) solution are injected in three to four seconds with the aid of a pressure apparatus.

Study Object	*Catheter Inserted*	*Position of Catheter Tip*
Whole circulation through heart and large vessels	Through a cubital vein	Vena cava superior
Auricular septum	»	Left auricle if possible
Right ventricle	»	Right ventricle
Pulmonary artery	»	Pulmonary artery
Left auricle and ventricle	»	»
Aorta in children	»	»
Aorta in adults	Through radial artery	
a) patent ductus	—	Middle part of ascendant aorta
b) coarctation	—	Just below origin of innominate artery

In cases of coarctation the catheter can be replaced by a cannula inserted through the right common carotid artery. In these cases 50 per cent solution should be used.

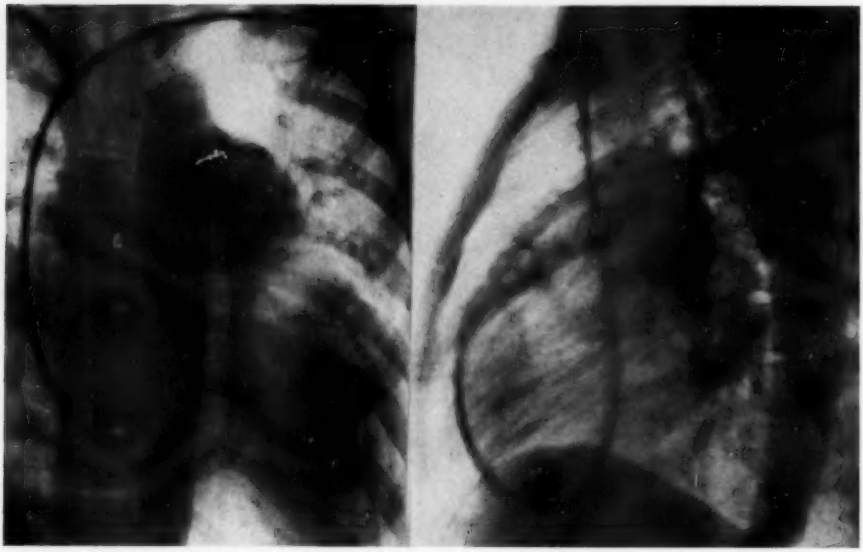


Fig. 10 a. Fig. 10 b.

Fig. 10. Female aged 10. Patent ductus. Frontal and lateral views. During catheterization for measurement of pressure and taking of samples for blood gas analysis, the catheter went into the aorta. The technical equipment we use making it possible for us to take advantage of this situation we injected contrast solution into the aorta and obtained a picture of the ductus. Thirty-five cc. of a 70 per cent umbradil solution were injected in three seconds.

SUMMARY

The authors describe their method of angiocardiography. The contrast solution is injected with a pressure apparatus through a catheter directly into the cardiac chamber or vessel it is wanted to study. The method, which could be called *selective angiocardiography*, is based on the method described by CHAVEZ, DORBECKER and CELIS for the right side of the heart and by RADNER and the authors themselves for the aorta.

ZUSAMMENFASSUNG

Verff. beschreiben ihre angiokardiographische Methode. Das Konstrastmittel wird mit einem Druckapparat durch einen Katheter direkt in die zu untersuchende Herzkammer oder das fragliche Gefäss eingespritzt. Die Methode, die man *selektive Angiokardiographie* nennen könnte, stellt eine weitere Entwicklung der Methode dar, die von CHAVEZ, DORBECKER und CELIS für die rechte Herzhälfte und von RADNER und Verff. selber für die Aorta beschrieben wurde.

RÉSUMÉ

Les auteurs décrivent leur méthode d'angiocardiographie. La solution de contraste est injectée à travers une sonde, à l'aide d'un appareil à pression, directement dans la cavité cardiaque ou le vaisseau qu'on désire examiner. Cette méthode, qui mériterait l'appellation *d'angiocardiographie élective*, est basée sur celle qui fut décrite par CHAVEZ, DORBECKER et CELIS pour le cœur droit, et par RADNER et les auteurs eux-mêmes pour l'aorte.

REFERENCES

AXÉN, O. and LIND, J.: Om angiocardiografi på späda barn. Nord. Med. Tidskr. *38*: 1143. 1943.

— La Tecnica de la Angiocardiografía en los niños. Rev. Espaň. de Pediatr. *4:* 161. 1948.

BRODÉN, B., HANSON, H. E. and KARNELL, J.: Thoracic aortography. Acta Radiol. *29:* 181. 1948.

CASTELLANOS, A., PEREIRAS, R. and GARCIA, A.: La Angio-Cardiografía radio-opaca. Arch. Socied. Estud. Clín. Habana 1937.

CHAVÈZ, I., DORBECKER, N. and CELIS, A.: Direct intracardiac angiocardiography — its diagnostic value. Am. Heart Journ. *33:* 560. 1947.

JÖNSSON, G.: Thoracic aortography by means of a cannula inserted percutaneously into the common carotid artery. Acta Radiol. *31:* 376. 1949.

JÖNSSON, G., BRODÉN, B., HANSON, H. E. and KARNELL, J.: Visualization of patent ductus arteriosus Botalli by means of thoracic aortography. Acta Radiol. *30:* 81. 1948.

RADNER, S.: Thoracal aortography by catheterization from the radial artery. Acta Radiol. *29:* 178. 1948.

ROBB, G. P. and STEINBERG, I.: A practical method of visualization of the chambers of the heart, the pulmonary circulation and the great vessels in man. J. Clin. Invest. *17:* 507. 1938.

ROUSTHÖI, P.; Über Angiokardiographie. Acta Radiol. *14:* 419. 1933.

FROM THE I. ROENTGENDIAGNOSTIC DEPARTMENT OF SÖDERSJUKHUSET, STOCKHOLM, SWEDEN (CHIEF: DOCENT G. JÖNSSON)

THORACIC AORTOGRAPHY[1]

Observations on technical problems connected with the method and various risks involved in its use

by

Bror Brodén, Gunnar Jönsson and *Johan Karnell*

In two articles on thoracic aortography, published in this journal in 1948, the writers described the technique of this method of examination. They also discussed the indications for its use and presented a preliminary report of results obtained in a few cases of coarctation of the aorta and patent ductus arteriosus Botalli. We employed a technique originally worked out by RADNER and extended later, by the writers. According to this technique, the contrast medium is injected through a heart catheter inserted into the aorta by way of the radial artery in the right arm. One of the writers (JÖNSSON) later introduced a new method for performing thoracic aortography, namely, »thoracic aortography by means of a cannula inserted percutaneously into the common carotid artery».

According to Jönsson's percutaneous method, the contrast medium is injected into the anterior part of the arch of the aorta. This allows examination of a coarctation and we have therefore adopted this technique for our coarctation cases. In the examination of patent ductus Botalli it is often advisable to inject the contrast medium as close as possible to the aortic orifice, and in our Botalli cases we therefore make our aortographic examinations, as we have done previously, after injecting the contrast medium through a catheter. Our series of thoracic aortographies comprises 21 cases of coarctation and 15 cases of patent ductus Botalli. In addition, we have had a few cases of aneurysm. Our results have been satisfactory in the majority of the cases, but a number of technical problems have arisen, and we have had complications in a few cases.

[1] Read at the Meeting of the Northern Association for Medical Radiology, June 10—12, 1949; submitted for publication, July 27, 1949.

We therefore consider it advisable to present a report of our experiences with the method, more especially from the aspects of the technique and the risks involved.

In performing *thoracic aortography with a catheter* inserted through the right radial artery we have met with problems of three kinds, viz.:

1) *Vascular spasm.* Spasm sometimes occurs despite the fact that the patient has been treated in advance with spasmolytics. We have observed probable or certain vascular spasm in 4 patients, all of whom were women. In only one of these patients was the spasm of such severity as to prevent an examination from being carried out. In addition to an individual disposition in the patient, two factors in connection with the technical procedure seem to be of special significance in producing the arterial spasm: a) too large a catheter; b) too protracted manipulation with the catheter. It is advisable to inject the contrast medium rapidly when performing thoracic aortography. This is facilitated with a large catheter. In most instances we have used a no. 8 or no. 9 F. heart catheter, in a few cases a no. 10 F. A large catheter is, of course, particularly useful when the contrast medium is being injected manually. If one is in possession of an apparatus effecting a rapid injection of the medium through a finer catheter also, one is less dependent on the diameter of the catheter. In all probability, spasm can be avoided by using a catheter that can be introduced without dilating the artery.

2) *Difficulty in directing the catheter to the aorta.* The catheter should be inserted rapidly. The risk of arterial spasm is increased if the catheter has to be manipulated for a long time before it enters the aorta. While the catheter is being introduced its tip may pass into, or become caught at, the point of origin of arterial branches springing from the axillary or subclavian arteries. The subscapular artery and the vertebral artery are the largest of these arterial branches (Fig. 1). When coarctation of the aorta is present arteries forming part of the collateral circulatory system are dilated, and in patients with coarctation other arteries besides those just mentioned may be wide enough to permit the entrance and passage of a heart catheter. The difficulties that may arise through the tip of the catheter entering arterial branches may be overcome by raising the arm in an upward direction, or by pressing the hand firmly on the axilla; further, by rotating the catheter so as to alter the position of its curved tip it can be brought into the centre of the artery and can thus continue to move onward in the vessel. If the catheter tends to pass into the vertebral artery, an unusual occurrence when catheters of the diameter suitable for this type of work are used, the tendency can sometimes be counteracted by pressing firmly on the supraclavicular fossa with the thumb. In one of our patients the course of the innominate artery was such that the catheter would not pass

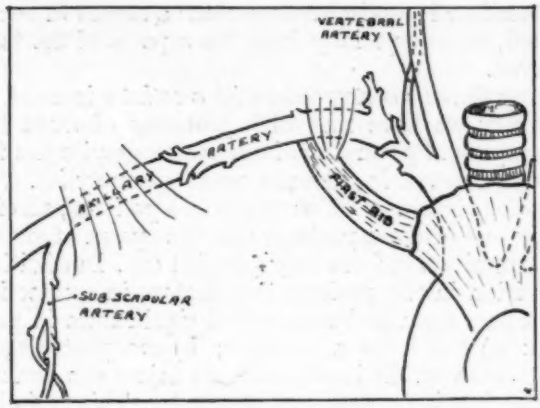


Fig. 1.

down into the ascending aorta but came to rest instead in the descending aorta. The possibility that anomalies may be present in peripheral arteries also must be taken into account in both coarctation of the aorta and patent ductus Botalli.

3) *Difficulty in bringing the tip of the catheter into the correct position.* In the typical cases, coarctation of the aorta is a stricture situated in the descending aorta on a level with Botal's ligament (isthmus). In atypical cases, there may be strictures in the arch of the aorta, multiple strictures, strictures combined with aneurysm, and so on. The anomalies are, however, always located in the aortic arch or the descending aorta. Thus, when coarctation cases are to be examined by contrast roentgenography the aortic arch and descending aorta are the parts that chiefly need to be studied. If the catheter technique is to be used for examining a coarctation it is therefore sufficient to insert the catheter just far enough to allow its tip to rest in the aorta at the origin of the innominate artery. If this is done, the aortic arch and descending aorta will be well filled with contrast medium while the ascending aorta will not always be satisfactorily filled (Fig. 2). In clinically established cases of patent ductus Botalli the aortographic examination — if it is considered indicated — can be performed in the same manner. If, on the other hand, it is a question of a differential diagnosis between patent ductus Botalli and some other interarterial communication,[1] the examination must be

[1] We have encountered two patients in whom it was found, at the clinical examination (which included cardiac catheterization and a gasometric analysis), that there was an interarterial communication proving, at operation, not to be patent ductus Botalli but a communication at the base of the aorta, probably an aneurysm in a sinus of Valsalva that had ruptured into the pulmonary conus or the right ventricle.

Fig. 2.

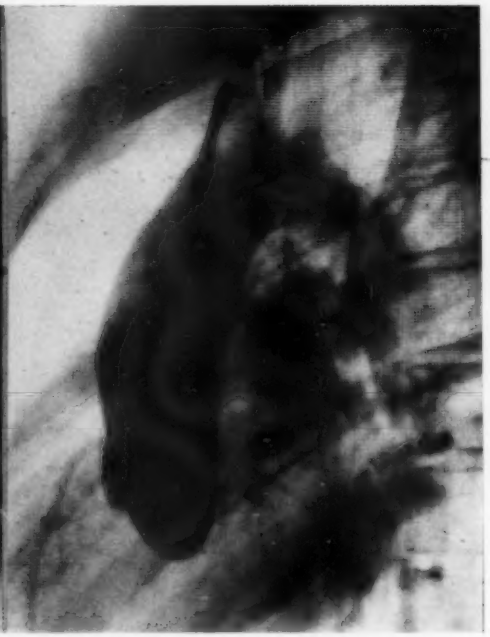


Fig. 3.

Fig. 2. Coarctation of the aorta. An atypical case. Thoracic aortography with a catheter. The tip of the catheter is situated at the point of origin of the innominate artery. The aortic arch and ascending aorta are filled with contrast medium. Three strictures are visualized, one in the arch of the aorta and two in the descending aorta (marked by arrows). This case, which is inoperable, demonstrates that in coarctation patients the aorta should be examined by contrast roentgenography before an operation is attempted.

Fig. 3. Patent ductus arteriosus Botalli. Thoracic aortography with a catheter, which was inserted far down into the ascending aorta. The whole of the thoracic aorta is filled with contrast medium. The substance is flowing through the patent ductus Botalli into the pulmonary artery. The ductus Botalli, which was found at operation to be very narrow, is not visualized. The coronary arteries are filled with contrast medium and are clearly visualized.

made in such a way as to ensure that all parts of the thoracic aorta are filled with the contrast medium, and the catheter should therefore be inserted far enough to permit the tip to pass well down into the ascending aorta (Fig. 3). The tip should not be placed *too low*. If it reaches too far down, the catheter can glide into one of the coronary arteries. This happened in one of our patients. When the injection was begun the cath-

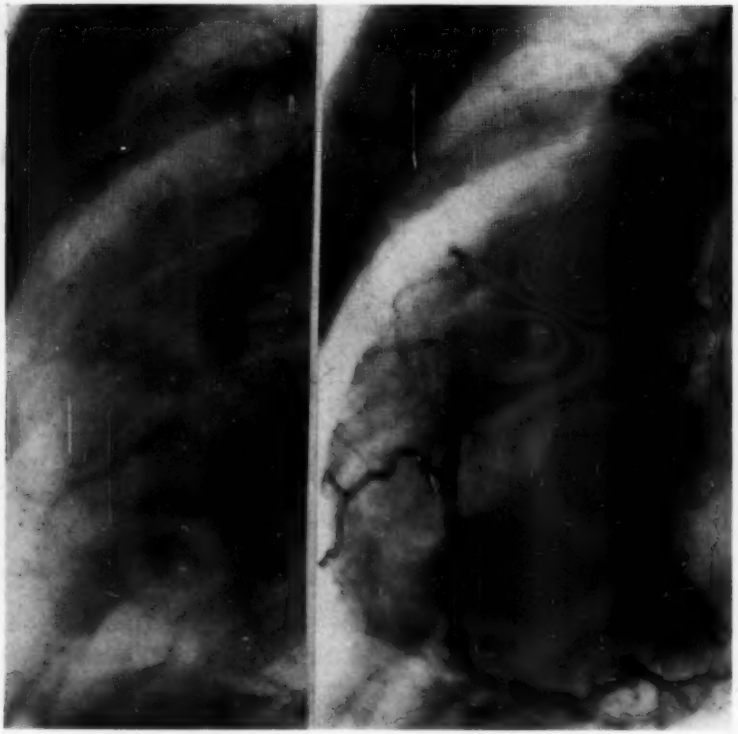


Fig. 4. Fig. 5.

eter lay in the right coronary artery (Figs. 4, 5 and 6). The patient suffered no pain that could conceivably have been due to this technical mishap. An electrocardiogram that was made during the aortographic examination revealed slight tachycardia but there were no other disturbances. It is probable that, in a case of this kind, the catheter recoils without difficulty out of the coronary vessel when the substance is injected, but in any case the catheter should be placed in such a position that a complication of the type described here is avoided. If the catheter lies *too high up*, another complication can arise. Owing to the increase in pressure that takes place in the catheter during the injection, the catheter strives to straighten itself out and it may then be flung over into the descending aorta, with the result that some of the contrast medium is injected into this part of the vessel (Figs. 7, 8 and 9).

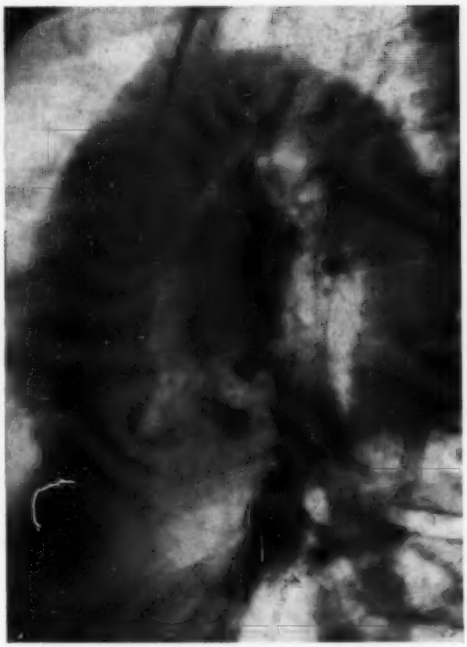


Fig. 6.

Figs. 4, 5 and 6. Patent ductus arteriosus Botalli. Thoracic aortography with a catheter. The catheter has been inserted *too far* in. Fig. 4: The tip of the catheter lies in the left coronary artery, which is seen to be filled with contrast medium. Fig. 5 (the picture was taken about 1 second later than fig. 4): Heart veins are filled with contrast medium. The tip of the catheter lies in the bulb of the aorta. Fig. 6: The whole of the thoracic aorta is filled with contrast medium. The substance is passing through the ductus Botalli into the pulmonary artery.

In the case of *aortography with a cannula*, one detail in particular is important to remember in connection with the puncturing. When a double cannula is used for the puncture, and arterial blood flows into the inner cannula, this is not a sure sign that the outer cannula also has passed into the artery. The double cannula must then be pushed in still further, perhaps even for such a distance that the flow of blood in the inner cannula ceases. It is usually a simple matter to introduce the outer cannula into the aortic arch with the aid of a guide thread. We were unsuccessful in doing this in one of our patients; at a later examination, using a different technique, this was found to be due to the fact that the course of the carotid and innominate arteries was abnormal (Fig. 10). It is most important that the tip of the cannula should be pushed right down into the aorta. With the aid of a guide through the cannula, it is possible to feel the inferior wall of the aortic arch and when the lengths of the cannula and guide are known it is possible to calculate how far the cannula should be inserted. In order to ensure that the aortic arch will be well filled with contrast medium the tip of the can-

Fig. 7.

Fig. 8.

Fig. 9.

Figs. 7, 8 and 9. Thoracic aortography with a catheter. The tip of the catheter lies *too far up* in the ascending aorta. During the injection, the catheter straightens itself out and is flung over into the descending aorta (fig. 9).

Fig. 10. Fig. 11.

Fig. 10. In this case, an attempt at thoracic aortography with a cannula was unsuccessful. At a subsequent angiocardiographic examination it was observed that the course of the innominate and carotid arteries was abnormally curved (arrows). This explained why the cannula could not be inserted into the aorta.

Fig. 11. See under figs. 12 & 13.

nula should be placed well towards the front and well towards the side; this can be achieved by holding the outer end of the cannula in a dorsal and medial direction (Figs. 11, 12 and 13).

The amount and concentration of the contrast medium. In connection with thoracic aortography, a not inconsiderable amount of contrast medium passes through the carotid arteries and up into the cerebral blood vessels. In one of our cases the contrast medium was injected by mistake into the innominate artery instead of into the aorta. The patient got epileptiform attacks and hemiparesis, the symptoms disappearing completely within four days. The chief cause of this complication was, of course, incorrect placing of the cannula, which resulted in too strong a concentration of contrast medium in the cerebral blood vessels. But even when the injection is made into the aorta the risk of cerebral complications should be borne in mind, and because of this risk caution should be exercised when deciding on the amount and concentration of contrast me-

Fig. 12.

Fig. 13.

Figs. 11, 12 and 13. Surgically treated coarctation of the aorta with aneurysm in the operative field. Thoracic aortography with a cannula. The tip of the cannula lies in the most suitable position for obtaining good visualization of the aortic arch, namely, as far to the side and front as possible. The right coronary artery, which is marked with an arrow, is filled with contrast.

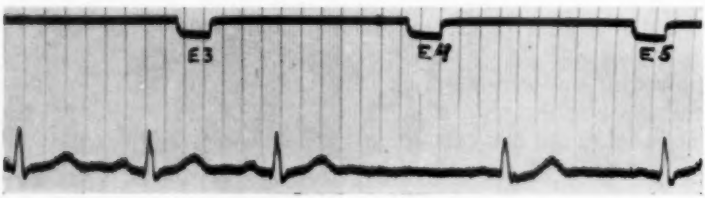


Fig. 14. The same case. An electrocardiogram taken during the aortographic examination. The exposures of the films are marked E 3, E 4, and so on.

dium to be used, as well as the rate of injection. We have used Diodrast and other media of the Diodrast type (Umbradil, Dijodon) in our investigations. Signs of brain damage, in the form of epileptiform spasms, have been observed in connection with cerebral angiography, which is

performed with these contrast media in solutions of up to 50 per cent. According to LINDGREN, such complications tend to occur particularly in epileptics and in patients with hypertensive encephalopathy. BROMAN and OLSSON, in an experimental study of »the tolerance of cerebral blood vessels to a contrast medium of the Diodrast group», have demonstrated that the brain damage arises as a result of a permeability disturbance. The same authors have also tested various other drugs that are available on the market, among others those we have used for our thoracic aortographies (Diodrast, Umbradil, Dijodon). Of these, Umbradil was said to be the least injurious.

In the majority of our cases we have used a 70 per cent solution and have injected 50 cc. The risk of cerebral complications perhaps is especially great in coarctation of the aorta, owing to the nature of the complaint, which, among other things, produces hypertension in the upper half of the body. We have therefore begun to use a 50 per cent solution for our coarctation cases, injecting, instead, a slightly larger amount. If the injection rate is not altered a lower concentration of contrast medium will be achieved with this technique. This lower concentration seems, however, to give adequate opacity of the aorta.

Injection rate. The strong resistance in the catheter or the cannula makes manual injection of contrast medium impossible. We use a specially constructed pressure apparatus (see JÖNSSON, Acta radiol. 31: 376, 1949) and inject 50—80 cc. in 3—5 seconds. For reasons already discussed in this paper, the injection should not be carried out too quickly in coarctation cases.

Radiographic technique. We use an automatic cassette changer that exposes 1 pair of plates a second (anteroposterior and lateral views).[1] One pair of pictures is taken before the injection of the contrast medium is begun. It sometimes happens that one or several plates are exposed during a ventricular systole, and the contrast medium in the ascending aorta is then flushed away by blood pouring from the heart. In the case illustrated in figures 11—13 there is no sign of contrast medium in the bulb of the aorta in figure 12. The right coronary artery is, however, filled with contrast, indicating that the bulb of the aorta had been filled at an earlier stage of the injection. An explanation of this phenomenon is furnished by an electrocardiogram taken at the same time; in figure 13 the picture was in all probability taken during a ventricular systole (at E. 3 on the EKG) while the picture taken about 1 second later (E. 4 on the EKG) — during a long pause between the ventricular complexes — was exposed after the aortic valves had been closed for a comparatively long time. The aorta is well filled with contrast medium in this picture. To obtain pictures from suitable heart phases, namely, immediately

[1] The cassette changer is of the same type as that used earlier by AXÉN and LIND.

before the aortic valves open, it would, of course, be desirable to arrange for the exchange and exposure of films under the control of electrocardiography. Probably, however, a slightly more rapid rate of exposure (3 pairs of films a second) would do away with the technical inconveniences described in this section.

SUMMARY

The writers discuss various technical problems associated with thoracic aortography and point out certain risks that can be avoided by employing a suitable technique.

ZUSAMMENFASSUNG

Verff. besprechen verschiedene technische Probleme, die die Aortographie in der Brusthöhle betreffen, und machen auf gewisse Gefahren aufmerksam, die sich durch Verwendung einer geeigneten Technik vermeiden lassen.

RÉSUMÉ

Les auteurs discutent de divers problèmes techniques à propos de l'aortographie thoracique et soulignent certains risques qui peuvent être évités en employant une technique appropriée.

REFERENCES

AXÉN, O. and LIND, J.: Om angiocardiografi på späda barn. Nord. Med. 38: 1143 (1948).

BRODÉN, B., HANSON, H. E. and KARNELL, J.: Thoracic aortography — Preliminary report. Acta radiol. 29: 181 (1948).

JÖNSSON, G., BRODÉN, B., HANSON, H. E. and KARNELL, J.: Visualization of patent ductus arteriosus Botalli by means of thoracic aortography. Acta radiol. 30: 81 (1948).

JÖNSSON, G.: Thoracic aortography by means of a cannula inserted percutaneously into the common carotid artery. Acta radiol. 31: 376 (1949).

BROMAN, T. and OLSSON, OLLE: The tolerance of cerebral blood-vessels to a contrast medium of the Diodrast group. Acta radiol. 30: 326 (1948).

—, Experimental study of contrast media for cerebral angiography with reference to possible injurious effects on the cerebral blood-vessels. Acta radiol. 31: 321 (1949).

LINDGREN, E.: The technique of direct (percutaneous) cerebral angiography. Brit. J. Radiol. 20: 326 (1947).

RADNER, S.: Thoracal aortography by catheterization from the radial artery. Acta radiol. 29: 178 (1948).

Index to Volume XXXII

Roentgen Diagnostics

Nervous System

Pag.

Herniated discs 60, 287
Intracranial haemorrhages 249
Myelography 60, 428
Glioma in cerebral hemispheres 461

Digestive Tract

Peptic ulcer of oesophagus 193
Infantile pyloric stenosis 435
Gallbladder 468

Heart and Vessels

Tuberculoma simulating cardiac aneurysm 73
Auricular movements 121
Calcified ductus Botalli persistens 173
Angiography in intracranial haemorrhages 249
Subclavian angiography 359
Phlebography of lower extremities 375
Selective angiocardiography 486
Thoracic aortography 498

Lungs, Pleura and Mediastinum

Frontal sinuses in bronchiectasis 185
Bronchography with viscous Umbradil 471

Diseases and Fractures of Bones and Joints

Herniated discs 60, 287
Hand-Schüller-Christian's disease 71, 89
Letterer-Siwe's disease 89
Eosinophilic granuloma 89
Dyschondroplasia 169
Fusion of vertebrae 404
Lipochondrodystrophie (Hurler's Syndrom) 439
Impression fractures in caput humeri 455
Sella turcica in glioma 461

Urogenital System

Utriculus prostaticus 28
Hydronephrosis 113
Renal tuberculosis 129

Ear, Nose and Throat

Frontal sinuses in bronchiectasis 185

Radiotherapy

Malignant melanoma of skin 33
Inflammatory conditions of tonsils 66

Pag.

Elektronenschleuder (Betatron) 145
Intracranial gliomas 210
Intraoral mucous- and salivary gland tumours 229
Cancer of oesophagus 304
Extramedullary plasmocytomas 365
Wide field irradiation 407

Hormone Therapy

Testosterone propionate in breast cancer 159

Protection and Injuries

Three cases of irradiation injuries 17

Radiobiology

Ester sulphuric acids in stroma connective tissue 11
Wide field irradiation and the platelet count 407

Cancerology

Dental prostheses and carcinoma 259

Technique

Roentgen Examination

Cineroentgenography 81
Tomography for curved surfaces 177
Angiography 249, 359
Electrokymography 276
Viscous Umbradil 317, 471
Phlebography 375
Fine structures in roentgenogram 391
Abrodil in myelography 428
Axial projection of gallbladder 468
Selective angiocardiography 486
Thoracic aortography 498

Radiotherapy

Elektronenschleuder (Betatron) 145
Rotation Treatment 304

Personality

Bibliographie du Professeur Gösta Forssell 337

Obituary

Alfred Ernest Barclay 1

List of Authors

Andersen, Poul E., 159, 304, 365
Andersson, Ture, 121, 276

Brodén, Bror, 486, 498
Brown, W. M. Court, 407

Denstad, Torfinn, 428

Edling, Lars, 1
Edling, Nils P. G., 28
Engeset, Arne, 210

Forssell, Gösta, 337

Gay, Roland, 129
Gidlund, Åke S., 81

Hansen, Poul Bjerre, 89
Hellström, B., 471
Hobæk, Andreas, 229, 259
Holmgren, Hj., 471
Hultberg, Sven, 17, 66
Husebye, O. W., 173
Højensgård, I. C., 375

Jönsson, Gunnar, 486, 498

Karnell, Johan, 486, 498
Kierulf, Erling, 169
Knutsson, Folke, 60, 404
Kovács, Ákos, 287
Krebs, Carl, 304

Lindblom, Knut, 113, 468
Liverud, Kjell, 73

Mellbye, Åke H., 71
Morales, Olallo, 317

Nielsen, Howard, 304
Nordmark, Bengt, 461
Notter, Gustaf, 439

Paatero, Yrjö V., 177

Radner, Stig, 359
Resink, J. E. J., 391

Sylwan, Tore, 455
Sylvén, Bengt, 11, 33

Thomsen, Gregers, 193
Torgersen, Johan, 185, 435

Wachsmann, F., 145
Wickbom, Ingmar, 249

Å, see A

Ö, Ø, see O